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=> d l8
L8 HAS NO ANSWERS
L8                STR
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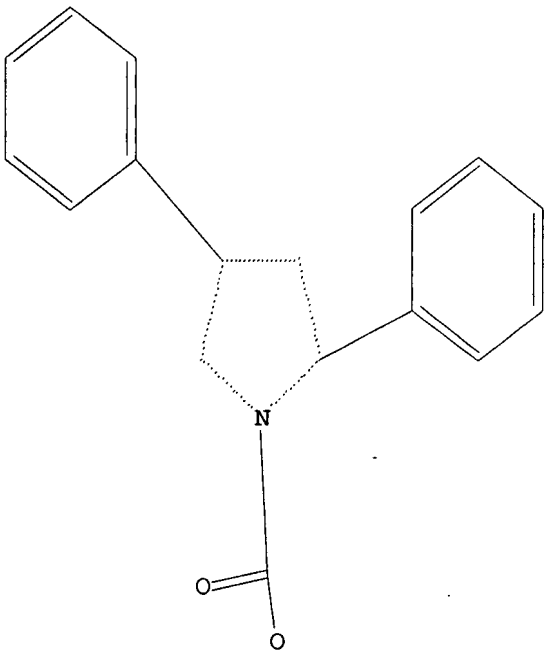

Structure attributes must be viewed using STN Express query preparation.

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=> d his

     (FILE 'HOME' ENTERED AT 09:59:11 ON 02 MAY 2007)

     FILE 'REGISTRY' ENTERED AT 09:59:17 ON 02 MAY 2007
L1                STRUCTURE UPLOADED
L2             50 S L1
L3           3670 S L1 SSS FULL
                  SAV TEM FBR517576/A L3
L4                STRUCTURE UPLOADED
L5             13 S L4 SAM SUB=L3
L6            236 S L4 SSS FULL SUB=L3
                  SAV TEM L6 10517576/A NAR517576/A

     FILE 'CAPLUS' ENTERED AT 10:04:01 ON 02 MAY 2007
L7             64 S L6
                  SAV TEM L7 ANS517576/A

     FILE 'STNGUIDE' ENTERED AT 10:04:55 ON 02 MAY 2007

     FILE 'REGISTRY' ENTERED AT 10:05:49 ON 02 MAY 2007
L8                STRUCTURE UPLOADED
L9              3 S L8  SUB=L6 SAM
L10            99 S L8 SSS FULL SUB=L6
                  SAV TEM N2517576/A L10

     FILE 'CAPLUS' ENTERED AT 10:07:34 ON 02 MAY 2007
L11            42 S L10
                  SAV TEM L11 AN2517576/A
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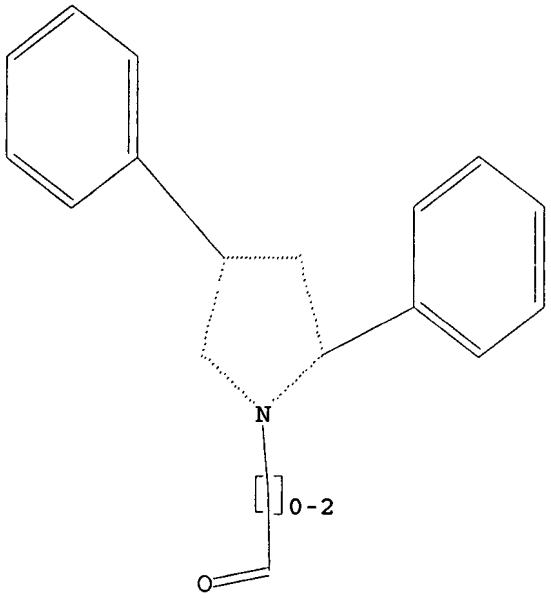
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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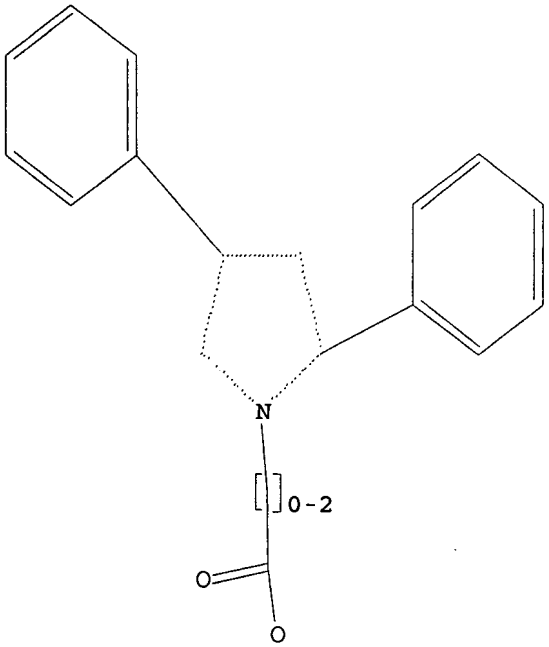
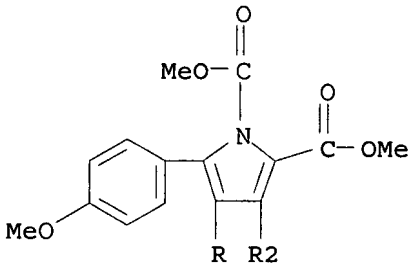
L4 HAS NO ANSWERS
L4 STR

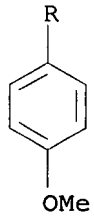


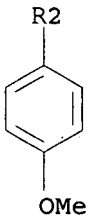
Structure attributes must be viewed using STN Express query preparation.

L11 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1319216 CAPLUS
DN 146:229113
TI Regioselective couplings of dibromopyrrole esters
AU Handy, Scott T.; Zhang, Yanan
CS Department of Chemistry, Binghamton University, Binghamton, NY, 13902, USA
SO Synthesis (2006), (22), 3883-3887
CODEN: SYNTBF; ISSN: 0039-7881
PB Georg Thieme Verlag
DT Journal
LA English
AB The regioselectivity of the Suzuki couplings of several 4,5- and 3,4-dibromopyrrole-2-carboxylate esters was studied. In general, regioselectivity can be achieved for initial coupling at the more electron-deficient site (C5 and C3, resp.). At the same time, conversions are often modest (40-60%) and attempts to force the reactions to higher conversions often lead to competitive dicoupling. E.g., Suzuki coupling of 2-Et 1-Me 4,5-dibromo-1H-pyrrole-1,2-dicarboxylate with 4-methoxyphenyl boronic acid gave 2-Et 1-Me 4-bromo-5-(4-methoxyphenyl)-1H-pyrrole-1,2-dicarboxylate in 56% yield. There is some influence of steric effects on the selectivity of the reaction.
IT 924708-90-7P
RL: BYP (Byproduct); PREP (Preparation)
(regioselective Suzuki coupling of dibromopyrrole carboxylates)
RN 924708-90-7 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3,4,5-tris(4-methoxyphenyl)-, 1,2-dimethyl ester (CA INDEX NAME)

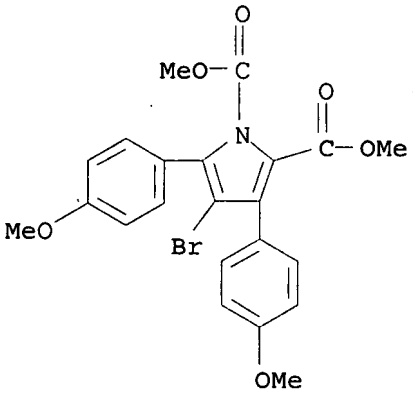
PAGE 1-A





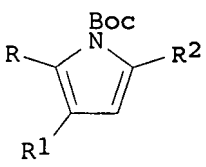


IT 924708-89-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(regioselective Suzuki coupling of dibromopyrrole carboxylates)
RN 924708-89-4 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 4-bromo-3,5-bis(4-methoxyphenyl)-, 1,2-dimethyl ester (CA INDEX NAME)

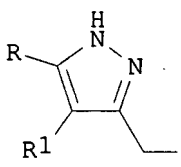


RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1224182 CAPLUS
DN 146:142558
TI Domino Cu-catalyzed C-N coupling/hydroamidation: a highly efficient synthesis of nitrogen heterocycles
AU Martin, Ruben; Rivero, Marta Rodriguez; Buchwald, Stephen L.
CS Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SO Angewandte Chemie, International Edition (2006), 45(42), 7079-7082
CODEN: ACIEF5; ISSN: 1433-7851
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 146:142558
GI



I



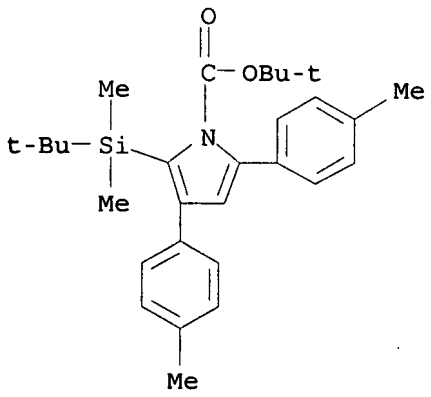
II

AB Boc-protected pyrroles and fused pyrroles and pyrazoles and fused pyrazoles with a variety of substituents are prepared by copper-catalyzed coupling and hydroamidation reactions of iodo- or bromoalkenynes and iodo- or bromoaryl alkynes with either tert-Bu carbamate or di-tert-Bu hydrazinedicarboxylate. Iodoenynes RCI:CR1C.tplbond.CR2 [R = EtCH2, Bu, Ph, 1-cyclohex-1-enyl, TIPSOCH2, MeO2C, TBS; R1 = H, EtCH2, 4-MeC6H4; RR1 = (CH2)3; R2 = H, EtCH2, Bu, BuCH2, 1-cyclohex-1-enyl, Ph, Cl(CH2)3, Me(CH2)7, 4-MeC6H4; TIPS = triisopropylsilyl; TBS = tert-butyldimethylsilyl] undergo coupling and hydroamidation reactions with BocNH2 in the presence of copper (I) iodide and N,N'-dimethylethylendiamine with cesium carbonate as a base in THF at 80° to give 1-Boc-pyrroles I [R = EtCH2, Bu, Ph, 1-cyclohex-1-enyl, TIPSOCH2, MeO2C, TBS; R1 = H, EtCH2, 4-MeC6H4; RR1 = (CH2)3; R2 = H, EtCH2, Bu, BuCH2, 1-cyclohex-1-enyl, Ph, Cl(CH2)3, Me(CH2)7, 4-MeC6H4; Boc = tert-butoxycarbonyl] in 52-95% yields; bromoenynes can be used when the reaction is performed in toluene (with potassium carbonate as the base) at 110°. Bromothienyl alkynes and an iodopyridinyl alkyne undergo copper-catalyzed cyclocondensation with tert-Bu carbamate under similar conditions to give thienopyrroles and a pyrrolopyridine, resp. Iodoenynes RCI:CR1C.tplbond.CR2 [R = H, EtCH2, Bu, Ph, PhCH2, TIPSOCH2; R1 = H, Et; RR1 = (CH2)3; R2 = H, EtCH2, BuCH2, Me(CH2)7, Ph, Cl(CH2)3, PhCH2O(CH2)2, EtO2C] undergo coupling and hydroamidation reactions with BocNH2 in the presence of copper (I) iodide and N,N'-dimethylethylendiamine with cesium carbonate as a base in THF at 80° followed by deprotection with F3CCO2H in CH2Cl2 to give pyrazoles II [R = H, EtCH2, Bu, Ph, PhCH2, TIPSOCH2; R1 = H, Et; RR1 = (CH2)3; R2 = H, EtCH2, BuCH2, Me(CH2)7, Ph, Cl(CH2)3, PhCH2O(CH2)2, EtO2C] in 66-93% yields. Ligands for the cyclocondensation are tested; only N,N'-dimethylethylenediamine and N,N'-dimethyl-trans-1,2-cyclohexanediamine are effective. The coupling and hydroamidation reactions require the presence of both the copper catalyst and ligand and added base. The prepns. of most of the iodoenyne and bromoenyne starting materials (as well as those of the bromothienyl alkynes and the iodopyridinyl alkyne) are described. Amine and hydrazine coupling products with an iodoenyne and a alkylidenedihydropyrazoledicarboxylate intermediate in the preparation of a pyrazole are isolated, supporting a coupling-hydroamidation pathway (rather than a hydroamidation-coupling pathway) for the reaction.

IT 919123-93-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyrroles by copper-catalyzed cyclocondensation (coupling/hydroamidation) reactions of a carbamate with iodoenynes and bromoenynes)

RN 919123-93-6 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2-[(1,1-dimethylethyl)dimethylsilyl]-3,5-bis(4-methylphenyl)-, 1,1-dimethylethyl ester (CA INDEX NAME)



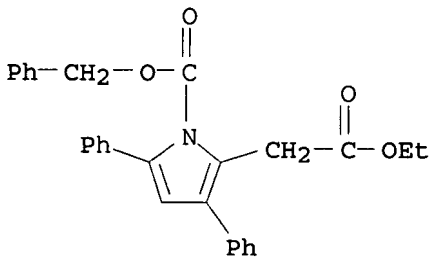
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:725314 CAPLUS
DN 145:292812
TI Efficient Synthesis of 1,3,5-Trisubstituted (Pyrrol-2-yl)acetic Acid Esters via Dual Nucleophilic Reactions of Sulfonamides or Carbamate with 4-Trimethyl-siloxy-(5E)-hexen-2-ynoates: Lewis Acid Catalyzed SN1 and Intramolecular Michael Addition
AU Ishikawa, Teruhiko; Aikawa, Toshiaki; Watanabe, Shinichiro; Saito, Seiki
CS Department of Medical and Bioengineering Science, Graduate School of Natural Science and Technology, Okayama University, Okayama, 700-8530, Japan
SO Organic Letters (2006), 8(17), 3881-3884
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
OS CASREACT 145:292812
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Benzyl carbamate or sulfonamides have proven to regioselectively attack 2-propynyl-allyl hybrid cations, generated by the action of TMSOTf on 4-(trimethylsiloxy)hex-5-en-2-ynoates, e.g., I, to afford conjugated 6-aminohex-4-en-2-ynoates, e.g., II, in which an intramol. amino-Michael reaction took place, leading to pyrroleacetates, e.g., III. The sulfonamides gave the pyrroleacetates by a one-pot process.
IT 908254-71-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyrroleacetates via regioselective Lewis acid-catalyzed nucleophilic substitution of (trimethylsiloxy)hexenynoates with sulfonamides or benzyl carbamate followed by intramol. Michael addition)
RN 908254-71-7 CAPLUS
CN 1H-Pyrrole-2-acetic acid, 3,5-diphenyl-1-[(phenylmethoxy)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:188863 CAPLUS
DN 144:432640
TI Kinesin spindle protein (KSP) inhibitors. Part 3: Synthesis and evaluation of phenolic 2,4-diaryl-2,5-dihydropyrroles with reduced hERG binding and employment of a phosphate prodrug strategy for aqueous solubility
AU Garbaccio, Robert M.; Fraley, Mark E.; Tasber, Edward S.; Olson, Christy M.; Hoffman, William F.; Arrington, Kenneth L.; Torrent, Maricel; Buser,

Carolyn A.; Walsh, Eileen S.; Hamilton, Kelly; Schaber, Michael D.; Fernandes, Christine; Lobell, Robert B.; Tao, Weikang; South, Vicki J.; Yan, Youwei; Kuo, Lawrence C.; Prueksaritanont, Thomayant; Slaughter, Donald E.; Shu, Cathy; Heimbrook, David C.; Kohl, Nancy E.; Huber, Hans E.; Hartman, George D.

CS Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA

SO Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 1780-1783
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:432640

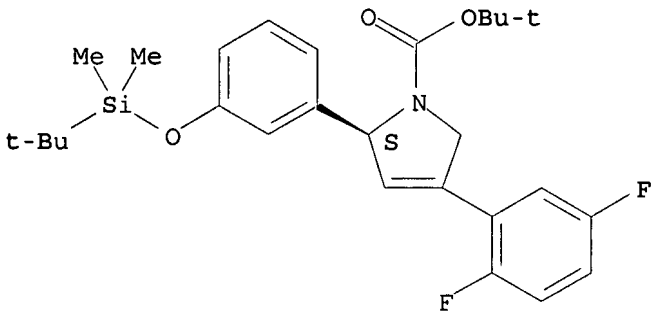
AB 2,4-Diaryl-2,5-dihydropyrroles have been discovered to be novel, potent and water-soluble inhibitors of KSP, an emerging therapeutic target for the treatment of cancer. A potential concern for these basic KSP inhibitors was hERG binding that can be minimized by incorporation of a potency-enhancing C-2 phenol combined with neutral N-1 side chains. Aqueous solubility was restored to these, and other, non-basic inhibitors, through a phosphate prodrug strategy.

IT 884651-21-2P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2,4-diaryl-2,5-dihydropyrroles as kinesin spindle protein (KSP) inhibitors with reduced hERG binding and phosphate prodrugs for aqueous solubility)

RN 884651-21-2 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]-2,5-dihydro-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

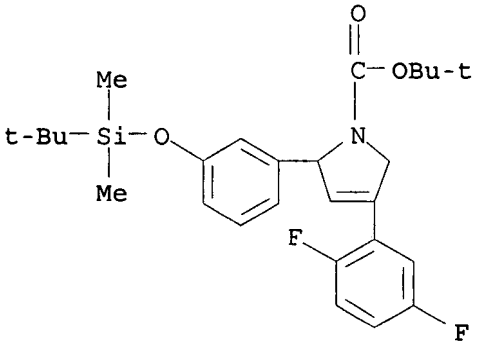
Absolute stereochemistry.



IT 639077-57-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2,4-diaryl-2,5-dihydropyrroles as kinesin spindle protein (KSP) inhibitors with reduced hERG binding and phosphate prodrugs for aqueous solubility)

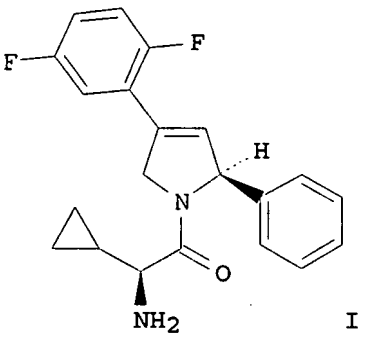
RN 639077-57-9 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]-2,5-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:188862 CAPLUS
DN 144:432639
TI Kinesin spindle protein (KSP) inhibitors. Part 2: The design, synthesis, and characterization of 2,4-diaryl-2,5-dihydropyrrole inhibitors of the mitotic kinesin KSP
AU Fraley, Mark E.; Garbaccio, Robert M.; Arrington, Kenneth L.; Hoffman, William F.; Tasber, Edward S.; Coleman, Paul J.; Buser, Carolyn A.; Walsh, Eileen S.; Hamilton, Kelly; Fernandes, Christine; Schaber, Michael D.; Lobell, Robert B.; Tao, Weikang; South, Victoria J.; Yan, Youwei; Kuo, Lawrence C.; Prueksaritanont, Thomayant; Shu, Cathy; Torrent, Maricel; Heimbrook, David C.; Kohl, Nancy E.; Huber, Hans E.; Hartman, George D.
CS Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 1775-1779
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 144:432639
GI



I

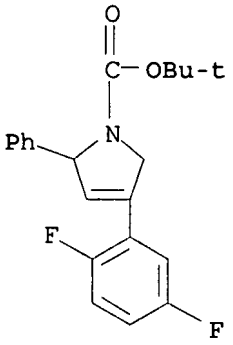
AB The development of nonracemic 1-acyl-2-phenyl-4-(2,5-difluorophenyl)-2,5-dihydropyrroles such as I as inhibitors of kinesin spindle protein (KSP) is described. Modification of the pyrazoline core of the lead compound to a dihydropyrrole core followed by introduction of basic amide and urea moieties yields compds. with enhanced potency and aqueous solubility which cause mitotic arrest of A2780 human ovarian carcinoma cells with EC50 values of < 10 nM. The binding of 1-acyl-2-phenyl-4-(2,5-difluorophenyl)-2,5-dihydropyrroles to KSP and to the potassium channel hERG is compared to

those of the corresponding 1-acyl-5-phenyl-3-(2,5-difluorophenyl)-4,5-dihydropyrazoles. The pharmacokinetics for I in rats, dogs, and monkeys are determined Crystal structures of three dihydropyrroles bound to the allosteric site of KSP are determined by X-ray crystallog.

IT 635724-42-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-phenyl-4-(2,5-difluorophenyl)-1-acyl-2,5-dihydropyrroles and comparison of their inhibition of KSP and of mitosis and their binding selectivities for KSP over the potassium channel hERG to those of the corresponding pyrazolines)

RN 635724-42-4 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

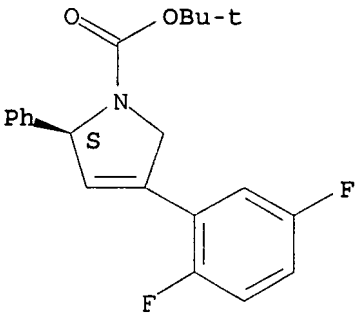


IT 635724-48-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nonracemic 2-phenyl-4-(2,5-difluorophenyl)-1-acyl-2,5-dihydropyrroles, their inhibition of KSP and of mitosis, and their binding selectivities for KSP over the potassium channel hERG)

RN 635724-48-0 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

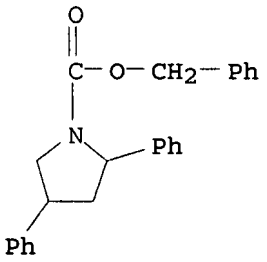
AN 2005:544172 CAPLUS

DN 143:229150

TI Imino-ene reaction of N-tosyl arylaldimines with α-methylstyrene: application in the synthesis of important amines

AU Pandey, Manoj K.; Bisai, Alakesh; Pandey, Ankur; Singh, Vinod K.

CS Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur, 208 016, India
SO Tetrahedron Letters (2005), 46(30), 5039-5041
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 143:229150
AB Copper(II) or tin(II) trifluoromethanesulfonate in combination with TMSCl effectively activates a C-H bond for the imino-ene reaction of N-tosylarylaldimines with α-methylstyrene. A wide variety of N-tosylarylaldimines RCH:NTs [R = (un)substituted Ph] were used to give homoallylamines RCH(NHTs)CH2CPh:CH2 in good to excellent yields under mild conditions. The imino-ene adduct was converted into a β-amino ketone PhCH(NHTs)CH2COPh. The synthesis of a 2,4-substituted pyrrolidine and a piperidine was also achieved from the imino-ene product via a Mitsunobu reaction and a Grubbs cyclization, resp.
IT 862659-16-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and reactions of homoallylamines)
RN 862659-16-3 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2,4-diphenyl-, phenylmethyl ester (9CI) (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:182653 CAPLUS
DN 142:280064
TI Preparation of dihydropyrrolecarboxamides as mitotic kinesin inhibitors for treating cancer
IN Coleman, Paul J.; Cox, Christopher D.; Garbaccio, Robert M.; Hartman, George D.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005019206	A1	20050303	WO 2004-US26012	20040811

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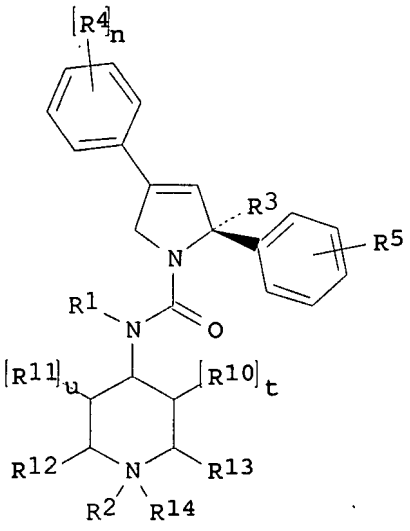
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

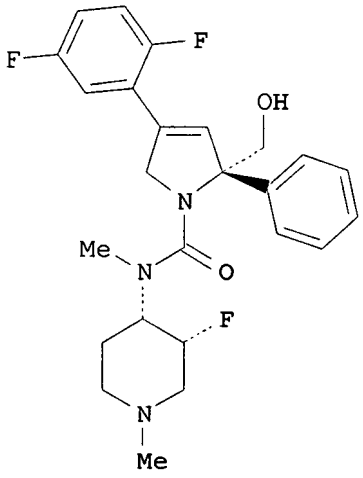
	US 2005043357	A1	20050224	US 2004-915743	20040811
	AU 2004266232	A1	20050303	AU 2004-266232	20040811
	CA 2534065	A1	20050303	CA 2004-2534065	20040811
	EP 1664026	A1	20060607	EP 2004-780791	20040811
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1839128	A	20060927	CN 2004-80023309	20040811
	BR 2004013580	A	20061017	BR 2004-13580	20040811
	JP 2007502774	T	20070215	JP 2006-523332	20040811
	US 2006234984	A1	20061019	US 2006-567676	20060209
	NO 2006001194	A	20060505	NO 2006-1194	20060314
PRAI	US 2003-495637P	P	20030815		
	US 2004-563580P	P	20040419		
	US 2003-512680P	P	20031020		
	US 2004-563586P	P	20040419		
	WO 2004-US25980	W	20040811		
	WO 2004-US26012	W	20040811		

OS MARPAT 142:280064

GI



I



II

AB The present invention relates to dihydropyrrole compds. I [R1, R2 = H, alkyl, aryl, etc.; R3 = H, alkyl, CH2OH, etc.; R4 = CO2H, halo, CN, etc.; R5 = H, halo, CN, etc.; R10, R11 = F, CH2F; R12, R13 = H, CH2F; R14 = absent, oxo; n = 0-3; t = 0-2; u = 0-1] that are useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. E.g., a multi-step synthesis of II, which showed an IC50 of ≤ 50 μM in kinesin ATPase in vitro assay, was given. The invention is also related to compns. which comprise these compds. I, and methods of using them to treat cancer in mammals.

IT 635724-48-0P

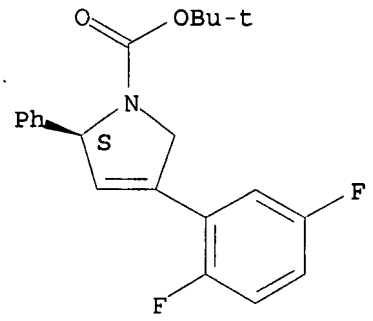
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of dihydropyrrolecarboxamides as mitotic kinesin inhibitors for treating or preventing cancer)

RN 635724-48-0 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:140806 CAPLUS
DN 142:240324
TI A preparation of pyrrolecarboxamide derivatives, useful as mitotic kinesin inhibitors
IN Coleman, Paul J.; Cox, Christopher D.; Garbaccio, Robert M.; Hartman, George D.
PA USA
SO U.S. Pat. Appl. Publ., 52 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005038074	A1	20050217	US 2004-916096	20040811
	WO 2005019205	A1	20050303	WO 2004-US25980	20040811
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	BR 2004013580	A	20061017	BR 2004-13580	20040811
	NO 2006001194	A	20060505	NO 2006-1194	20060314
PRAI	US 2003-495637P	P	20030815		
	US 2003-512680P	P	20031020		
	US 2004-563586P	P	20040419		
	WO 2004-US25980	W	20040811		

OS CASREACT 142:240324; MARPAT 142:240324
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of pyrrolecarboxamide derivs. of formula I [wherein: R1 is H, alkyl, aryl, or heterocyclyl, etc.; R2 is 4-piperidinyl derivative; R3 is H, alkyl, alkdiyl-OH, alkdiyl-O-alkyl, or alk(en/yn)diyl-C(O)-NH2, etc.; R4 is CO2H, halogen, CN, or OH, etc.; R5 is

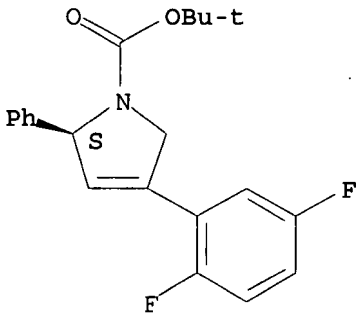
H, CO2H, CN, halogen, or OP(:O)(OH)2, etc.], useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. The invention is also related to compns. which comprise these compds., and methods of using them to treat cancer in mammals. For instance, pyrrolecarboxamide derivative II (kinesin ATPase in vitro assay: IC50 < 50 μM) was prepared via amidation of carbamoyl chloride III by amine IV (conversion of III to the product was >98%).

IT 635724-48-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolecarboxamide derivs. useful as mitotic kinesin inhibitors)

RN 635724-48-0 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:1156433 CAPLUS

DN 142:69166

TI Bicyclic dihydropyrrole compound mitotic kinesin inhibitors, and therapeutic use

IN Coleman, Paul J.; Neilson, Lou Anne

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

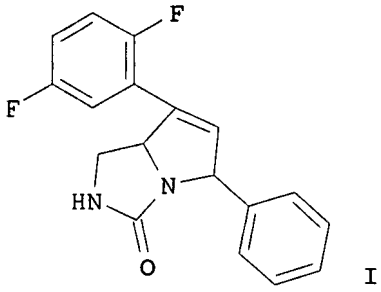
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004112699	A2	20041229	WO 2004-US18137	20040608
	WO 2004112699	A3	20050414		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004249138	A1	20041229	AU 2004-249138	20040608
	CA 2527533	A1	20041229	CA 2004-2527533	20040608
	EP 1635641	A2	20060322	EP 2004-776354	20040608
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

	CN 1805686	A	20060719	CN 2004-80016445	20040608
	JP 2007501863	T	20070201	JP 2006-533604	20040608
	US 2006142278	A1	20060629	US 2005-559855	20051207
PRAI	US 2003-477975P	P	20030612		
	WO 2004-US18137	W	20040608		

OS MARPAT 142:69166

GI



I

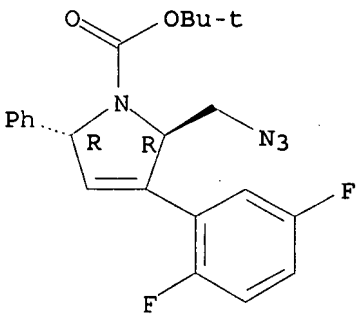
AB The invention discloses bicyclic dihydropyrrole compds. that are useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. The invention also discloses compns. which comprise these compds., and methods of using them to treat cancer in mammals. Preparation of compds., e.g. I, is described.

IT 812631-76-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(bicyclic dihydropyrrole compound mitotic kinesin inhibitors, and therapeutic use)

RN 812631-76-8 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2-(azidomethyl)-3-(2,5-difluorophenyl)-2,5-dihydro-5-phenyl-, 1,1-dimethylethyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

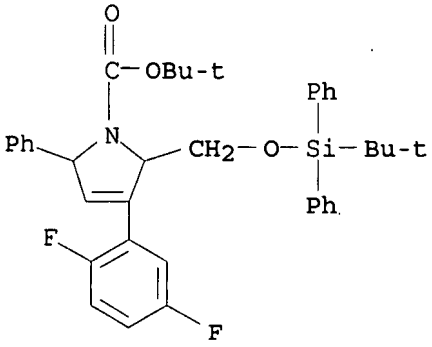


IT 812631-69-9P 812631-70-2P 812631-71-3P
812631-72-4P 812631-73-5P 812631-74-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bicyclic dihydropyrrole compound mitotic kinesin inhibitors, and therapeutic use)

RN 812631-69-9 CAPLUS

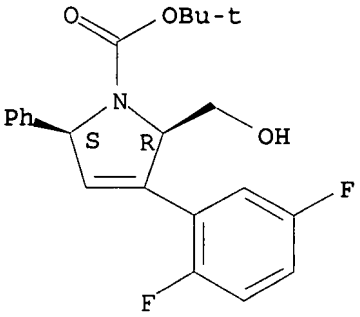
CN 1H-Pyrrole-1-carboxylic acid, 3-(2,5-difluorophenyl)-2-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-2,5-dihydro-5-phenyl-,

1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



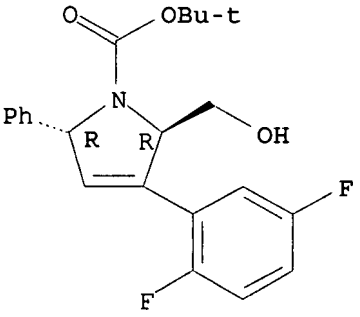
RN 812631-70-2 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 3-(2,5-difluorophenyl)-2,5-dihydro-2-(hydroxymethyl)-5-phenyl-, 1,1-dimethylethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



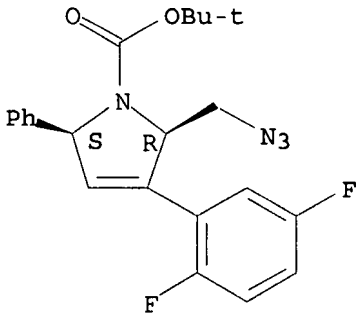
RN 812631-71-3 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 3-(2,5-difluorophenyl)-2,5-dihydro-2-(hydroxymethyl)-5-phenyl-, 1,1-dimethylethyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



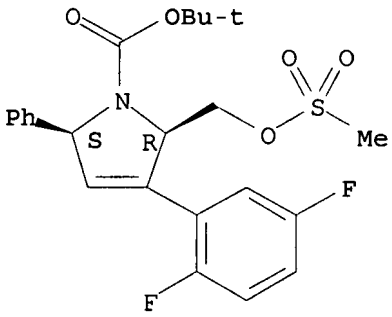
RN 812631-72-4 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2-(azidomethyl)-3-(2,5-difluorophenyl)-2,5-dihydro-5-phenyl-, 1,1-dimethylethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



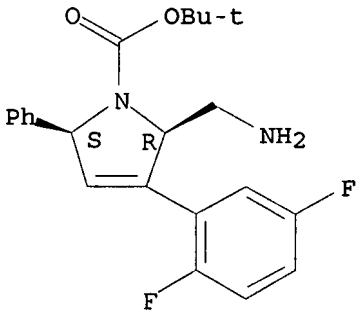
RN 812631-73-5 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 3-(2,5-difluorophenyl)-2,5-dihydro-2-[[(methylsulfonyl)oxy]methyl]-5-phenyl-, 1,1-dimethylethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 812631-74-6 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2-(aminomethyl)-3-(2,5-difluorophenyl)-2,5-dihydro-5-phenyl-, 1,1-dimethylethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L11 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1127483 CAPLUS
DN 142:74446
TI A preparation of pyrrole derivatives, useful as mitotic kinesin inhibitors
IN Fraley, Mark E.; Garbaccio, Robert M.; Hartman, George D.; Hoffman, William F.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004111193	A2	20041223	WO 2004-US18065	20040608
	WO 2004111193	A3	20050324		
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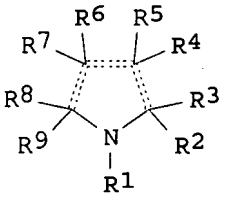
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004248160	A1	20041223	AU 2004-248160	20040608
	CA 2527582	A1	20041223	CA 2004-2527582	20040608
	EP 1636182	A2	20060322	EP 2004-754621	20040608
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	CN 1805928	A	20060719	CN 2004-80016354	20040608
	JP 2007505949	T	20070315	JP 2006-533588	20040608
	US 2006135594	A1	20060622	US 2005-559857	20051207
PRAI	US 2003-477995P	P	20030612		
	WO 2004-US18065	W	20040608		

OS MARPAT 142:74446
GI



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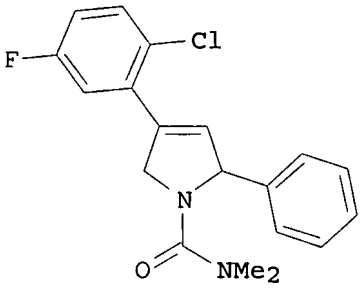
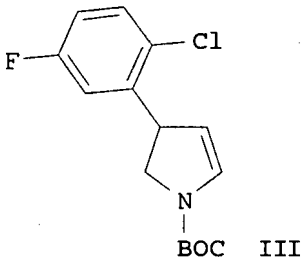


II



III

AB The invention relates to a preparation of pyrrole derivs. of formula I [wherein: R1 is (alkylene)0-1C(O)-alk(en/yn)yl, (alkylene)0-1C(S)-alk(en/yn)yl, or (alkylene)0-1-SO2-alkyl, etc.; R2 and R6 are independently selected from aryl, cycloalkyl, heterocyclyl, or aralkyl; R3, R4, R5, R7, R8, and R9 are independently selected from H, alk(en/yn)yl, aryl, or heterocyclyl, etc.], useful as mitotic kinesin

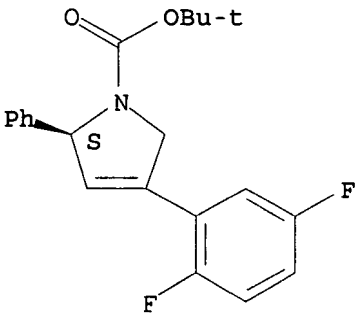
inhibitors (no biol. data). The invention compds. are useful for the treatment of proliferative diseases such as cancer, hyperplasia, restenosis, and immune disorders. For instance, pyrrolecarboxamide derivative II was prepared via phenylation of N-BOC-pyrrol derivative III by PhN2+•BF4-, N-deprotection, and N-carboxamidation by ClC(O)NMe2 (scheme 1).

IT 635724-48-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrole derivs. useful as mitotic kinesin inhibitors)

RN 635724-48-0 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

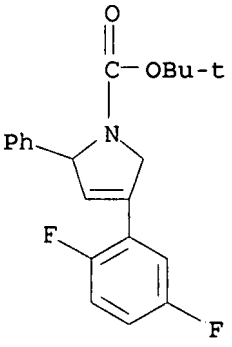
Absolute stereochemistry.



IT 635724-42-4P 639072-35-8P 639074-72-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrole derivs. useful as mitotic kinesin inhibitors)

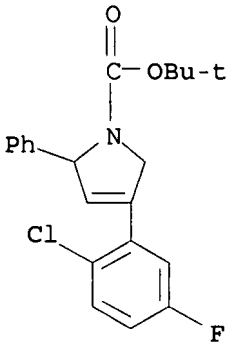
RN 635724-42-4 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

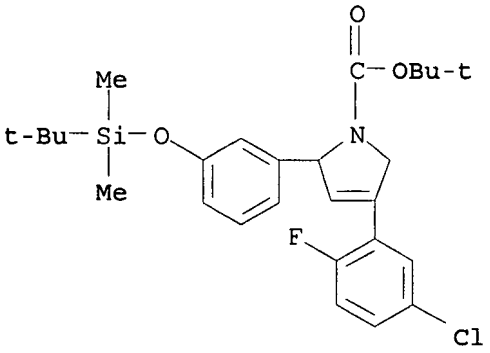


RN 639072-35-8 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2-chloro-5-fluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 639074-72-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(5-chloro-2-fluorophenyl)-2-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]-2,5-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



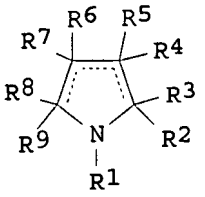
L11 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:857324 CAPLUS
DN 141:332040
TI Preparation of dihydropyrrole derivatives as mitotic kinesin inhibitors
IN Slaughter, Donald E.; Subramanian, Raju; Fraley, Mark E.; Prueksaritanont, Thomayant; Shu, Hong
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004087050	A2	20041014	WO 2004-US9027	20040324
	WO 2004087050	A3	20050324		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-458494P P 20030328
OS MARPAT 141:332040

GI



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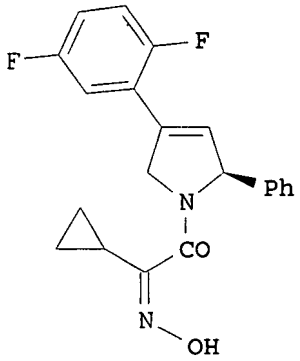


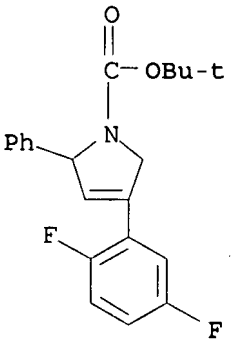
II

AB Dihydropyrrole compds. of formula I [R1 = COCRaNOH, COCRaNO2, etc.; Ra, R2, R6 = aryl, aralkyl, cycloalkyl, heterocyclyl; R3-R5, R7-R9 = H, alkyl, aryl, aralkyl, cycloalkyl, heterocyclyl, etc.] are prepared which are useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. The invention also related to compns. which comprise these compds., and methods of using them to treat cancer in mammals. Thus, II was prepared, and had IC50 ≤ 50 μM against kinesin motor domain.

IT 635724-42-4P 635724-48-0P 639072-35-8P
639074-72-9P 639075-47-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dihydropyrrole derivs. as antitumor agents)

RN 635724-42-4 CAPLUS

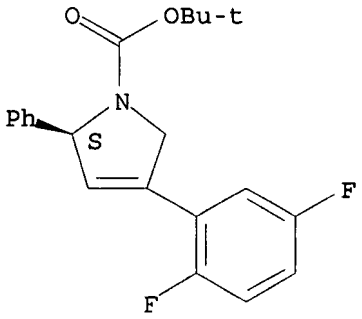
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



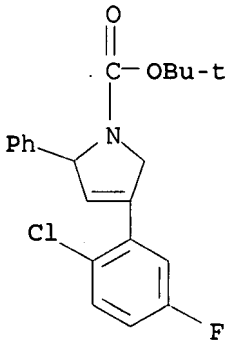
RN 635724-48-0 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

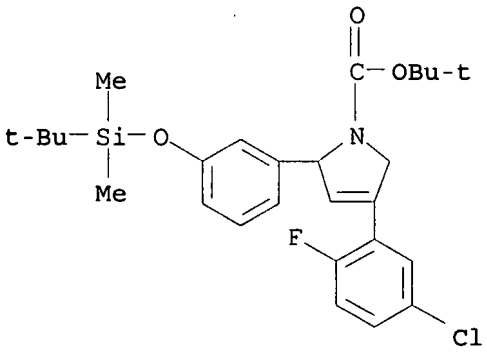
Absolute stereochemistry.



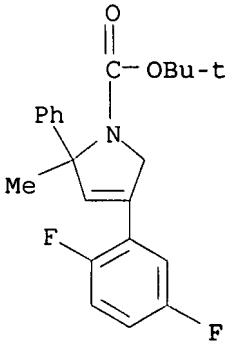
RN 639072-35-8 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2-chloro-5-fluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 639074-72-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(5-chloro-2-fluorophenyl)-2-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]-2,5-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 639075-47-1 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-methyl-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:368866 CAPLUS
DN 140:391193
TI Preparation of dihydropyrroles as mitotic kinesin inhibitors for treating cellular proliferative diseases
IN Breslin, Michael J.; Coleman, Paul J.; Cox, Christopher D.; Hartman, George D.; Mariano, Brenda J.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 178 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004037171	A2	20040506	WO 2003-US32405	20031014
	WO 2004037171	A3	20040708		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2500848	A1	20040506	CA 2003-2500848	20031014
	AU 2003287057	A1	20040513	AU 2003-287057	20031014
	EP 1556052	A2	20050727	EP 2003-777578	20031014
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006506456	T	20060223	JP 2005-501618	20031014
	US 2006100191	A1	20060511	US 2005-531495	20050415
PRAI	US 2002-419570P	P	20021018		
	US 2003-479712P	P	20030619		
	WO 2003-US32405	W	20031014		

OS MARPAT 140:391193
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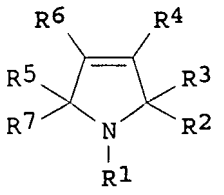

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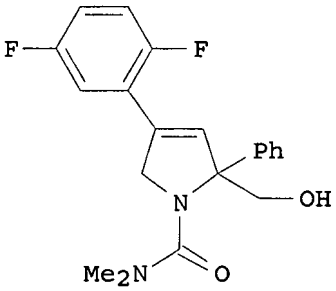


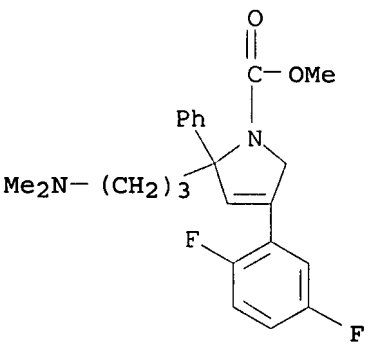
II

AB Title compds. I [wherein R1 = (un)substituted acyl(alkyl), carbamoyl(alkyl), sulfamoyl(alkyl), aryl, heterocyclyl, alkyl, etc.; R2 and R6 = independently (un)substituted aryl(alkyl), cycloalkyl, or heterocyclyl; R3 = (un)substituted alkoxyalk(en/yn)yl, carbamoylalk(en/yn)yl, alkylsulfonylalk(en/yn)yl, etc.; R4, R5, and R7 = independently H or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, perfluoroalkyl, arylalkyl, or heterocyclyl; or R5 and R7 are combined to form an oxo or sulfoxo; or pharmaceutically acceptable salt of stereoisomer thereof] were prepared for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity, and for inhibiting KSP kinesin. The invention is also related to compns. which comprise these compds., and methods of using them to treat cancer (no data). For instance, palladium catalyzed Suzuki coupling of 7a-phenyldihydro-1H-pyrrolo[1,2-c][1,3]oxazole-3,6(5H)-dione (multi-step preparation given) and 2,5-difluorophenylboronic acid afforded 6-(2,5-difluorophenyl)-7a-phenyl-5,7a-dihydro-1H-pyrrolo[1,2-c][1,3]oxazol-3-one. The pyrrolooxazolone was treated with NaOH in EtOH to give the (hydroxymethyl)pyrrole, which was O-protected with tert-butyldimethylsilyl chloride. Reaction of the pyrrole with triphosgene and dimethylamine, followed by deprotection using triethylamine trihydrofluoride in MeCN provided II. In a kinesin ATPase assay using a human KSP motor domain construct and microtubules from bovine brain tubulin, example compds. inhibited the ATPase hydrolysis reaction with IC50 ≤ 50 μM.

IT 686321-40-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(KSP inhibitor; preparation of dihydropyrroles as KSP inhibitors for treating proliferative diseases)

RN 686321-40-4 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2-[3-(dimethylamino)propyl]-2,5-dihydro-2-phenyl-, methyl ester (9CI) (CA INDEX NAME)

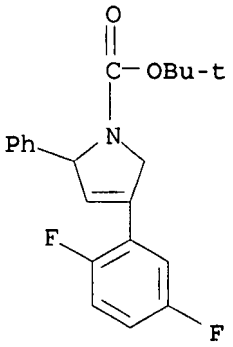


AN 2004:41221 CAPLUS
DN 140:107282
TI Crystal structure of human mitotic kinesin motor domain complexed with ligands and use of the three-dimensional structure in drug discovery
IN Buser-Doepner, Carolyn A.; Coleman, Paul J.; Cox, Christopher D.; Fraley, Mark E.; Garbaccio, Robert M.; Hartman, George D.; Heimbrook, David C.; Kuo, Lawrence C.; Huber, Hans E.; Sardana, Vinod V.; Torrent, Maricel; Yan, Youwei
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 290 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004652	A2	20040115	WO 2003-US21145	20030703
	WO 2004004652	A3	20041104		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2489562	A1	20040115	CA 2003-2489562	20030703
	AU 2003247891	A1	20040123	AU 2003-247891	20030703
	EP 1551962	A2	20050713	EP 2003-763258	20030703
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005537257	T	20051208	JP 2004-519930	20030703
	US 2006134767	A1	20060622	US 2006-520492	20060130
PRAI	US 2002-394313P	P	20020708		
	WO 2003-US21145	W	20030703		

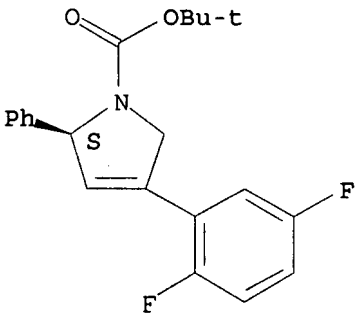
AB The present invention is directed to the identification, characterization and three-dimensional structure of a novel ligand binding site of kinesin spindle protein (KSP). Binding of ligands to the novel binding site result in a conformational change in the three-dimensional structure of the protein and a modulation of the activity of KSP. This conformational change in turn results in the formation of a novel binding pocket in the KSP protein, which comprises the novel binding site of the instant invention. Compns. and crystals of KSP motor domain with a KSP inhibitor bound to the protein at the novel ligand-binding site are also provided. The crystallized KSP motor domain is phys. analyzed by x-ray diffraction techniques. The resulting x-ray diffraction patterns are of sufficiently high resolution to be useful for determining the three-dimensional structure of inhibitor-bound KSP motor domain. Those atomic coordinates are useful in mol. modeling of related proteins and rational drug design of mimetics and ligands for KSP and related proteins. Methods of using the structure coordinates of KSP motor domain in complex with an inhibitor for the design of pharmaceutical compds. which inhibit the biol. function of KSP, particularly those biol. functions mediated by mol. interactions involving KSP are also disclosed.
IT 635724-42-4P 635724-48-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of kinesin ligands; crystal structure of human mitotic kinesin motor domain complexed with ligands and use of three-dimensional structure in drug discovery)
RN 635724-42-4 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-

, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 635724-48-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:1006949 CAPLUS
DN 140:42026
TI Preparation of dihydroindolylcarboxylates as mitotic kinesin inhibitors
IN Arrington, Kenneth L.; Fraley, Mark E.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 93 pp.
    CODEN: PIXXD2
DT Patent
LA English

INSTANT

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106417	A1	20031224	WO 2003-US18694	20030612
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2486215	A1	20031224	CA 2003-2486215	20030612
	AU 2003276005	A1	20031231	AU 2003-276005	20030612
	EP 1515949	A1	20050323	EP 2003-741969	20030612

	EP 1515949	B1	20070314		
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	JP 2005533063	T	20051104	JP 2004-513250	20030612
	US 2006063942	A1	20060323	US 2004-517576	20041209
PRAI	US 2002-388828P	P	20020614		
	WO 2003-US18694	W	20030612		

OS MARPAT 140:42026

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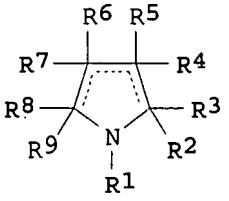

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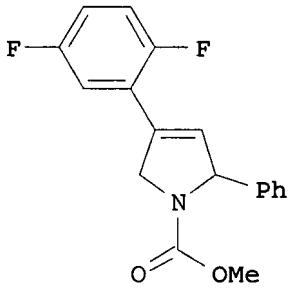


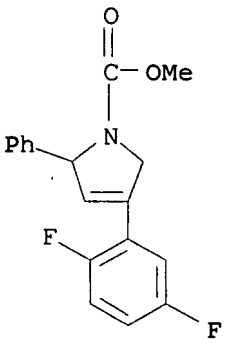
II

AB Title compds. I [R1 = carboxy; R2, R6 = aryl, arylalkyl, cycloalkyl, etc.; R3-5, R7-9 = H, alkyl, aryl, alk(en/yn)yl, etc.] are prepared For instance, tert-Bu 3-(2,5-difluorophenyl)-2,3-dihydro-1H-pyrrole-1-carboxylate (preparation given) is coupled to benzenediazonium tetrafluoroborate (CH3CN, Pd2dba3, NaOAc, 23°) to give tert-Bu 4-(2,5-difluorophenyl)-2-phenyl-2,5-dihydro-1H-pyrrole-1-carboxylate. This intermediate is deprotected (CH2Cl2, TFA) and converted to II (CH2Cl2, i-Pr2NEt, ClCO2Me). In a kinesin ATPase assay, example compds. exhibit IC50 ≤ 50μM. I are useful for treating cellular proliferative diseases, for treating disorders associated with KSP kinesin activity and for inhibiting KSP kinesin. The invention also related to compns. which comprise these compds. and methods of using them to treat cancer in mammals.

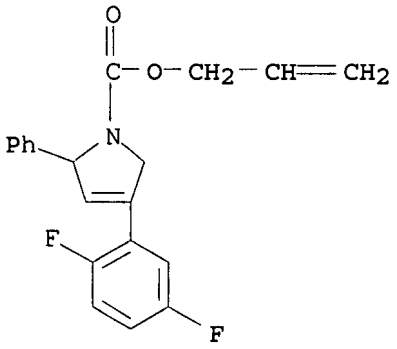
IT 635724-24-2P 635724-25-3P 635724-26-4P
635724-27-5P 635724-28-6P 635724-29-7P
635724-30-0P 635724-31-1P 635724-32-2P
635724-33-3P 635724-34-4P 635724-35-5P
635724-36-6P 635724-37-7P 635724-38-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dihydroindolylcarboxylates as mitotic kinesin inhibitors)

RN 635724-24-2 CAPLUS

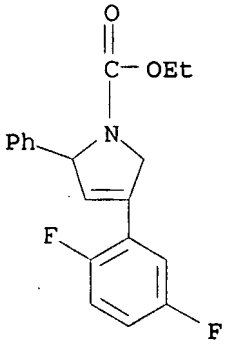
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, methyl ester (9CI) (CA INDEX NAME)



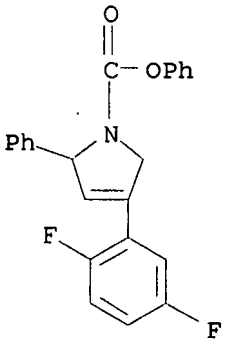
RN 635724-25-3 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 2-propenyl ester (9CI) (CA INDEX NAME)



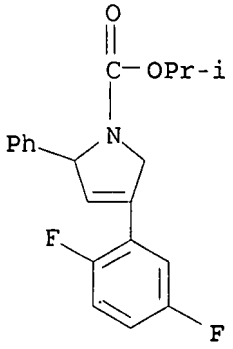
RN 635724-26-4 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 635724-27-5 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, phenyl ester (9CI) (CA INDEX NAME)

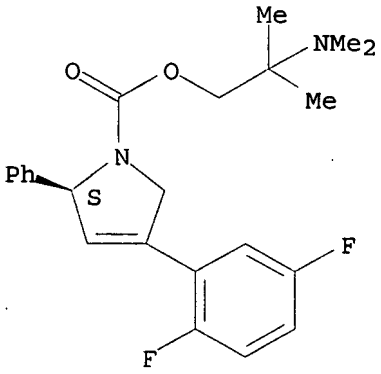


RN 635724-28-6 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)



RN 635724-29-7 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 2-(dimethylamino)-2-methylpropyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

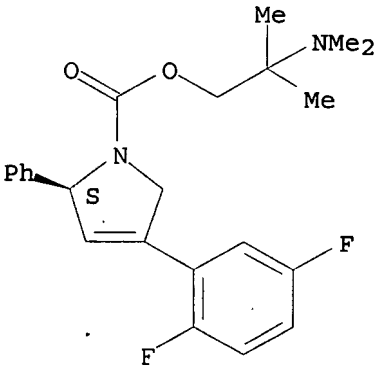


RN 635724-30-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 2-(dimethylamino)-2-methylpropyl ester, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

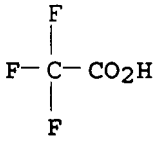
CRN 635724-29-7
CMF C23 H26 F2 N2 O2

Absolute stereochemistry.



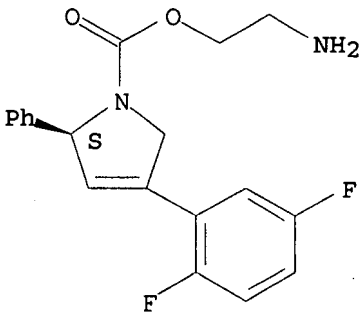
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 635724-31-1 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 2-aminoethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

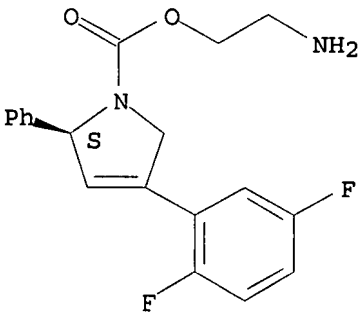


RN 635724-32-2 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 2-aminoethyl ester, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

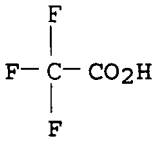
CRN 635724-31-1
CMF C19 H18 F2 N2 O2

Absolute stereochemistry.



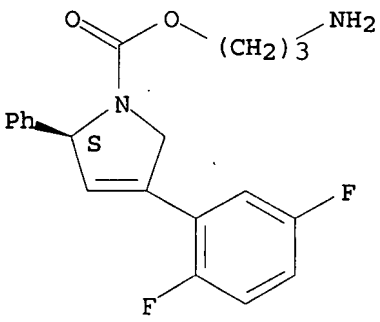
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 635724-33-3 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 3-aminopropyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

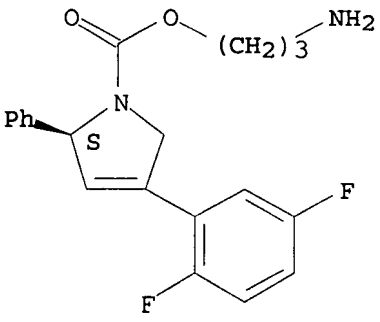


RN 635724-34-4 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 3-aminopropyl ester, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

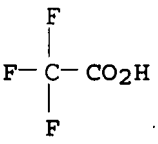
CRN 635724-33-3
CMF C20 H20 F2 N2 O2

Absolute stereochemistry.



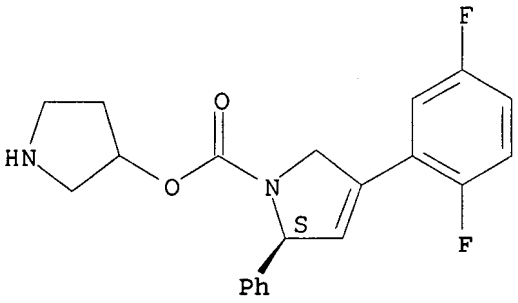
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 635724-35-5 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 3-pyrrolidinyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

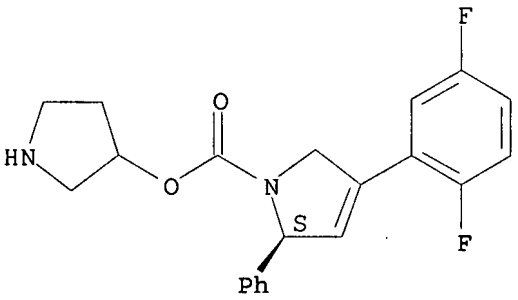


RN 635724-36-6 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 3-pyrrolidinyl ester, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

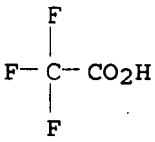
CRN 635724-35-5
CMF C21 H20 F2 N2 O2

Absolute stereochemistry.



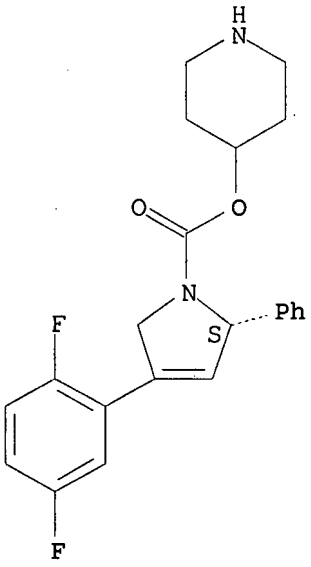
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 635724-37-7 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 4-piperidinyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

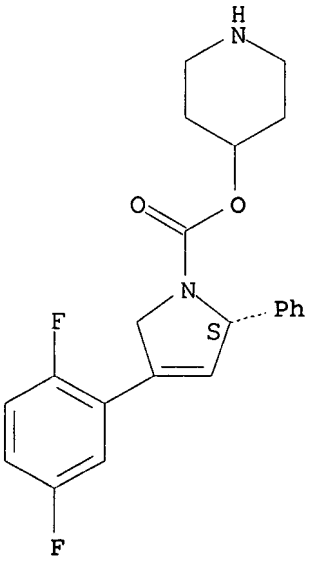


RN 635724-38-8 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 4-piperidinyl ester, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

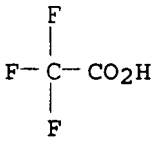
CRN 635724-37-7
CMF C22 H22 F2 N2 O2

Absolute stereochemistry.

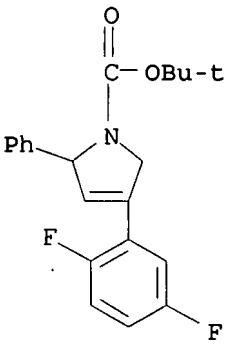


CM 2

CRN 76-05-1
CMF C2 H F3 O2

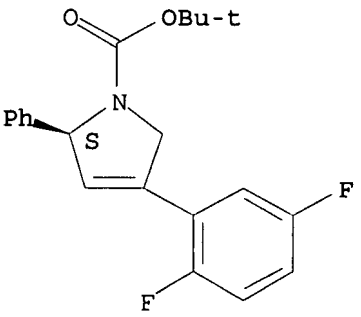


IT 635724-42-4P 635724-48-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dihydroindolylcarboxylates as mitotic kinesin inhibitors)
RN 635724-42-4 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 635724-48-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:1006780 CAPLUS
DN 140:77020
TI Preparation of pyrrole derivatives as mitotic kinesin inhibitors
IN Arrington, Kenneth L.; Coleman, Paul J.; Cox, Christopher D.; Fraley, Mark E.; Garbaccio, Robert M.; Hartman, George D.; Hoffman, William F.; Tasber, Edward S.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 401 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003105855	A1	20031224	WO 2003-US18482	20030612
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	AU 2003245453	A1	20031231	AU 2003-245453	20030612
	BR 2003011784	A	20050308	BR 2003-11784	20030612
	EP 1515724	A1	20050323	EP 2003-739093	20030612
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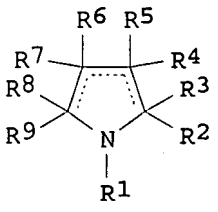
	CN 1674906	A	20050928	CN 2003-819318	20030612
	JP 2005536479	T	20051202	JP 2004-512758	20030612
	ZA 2004009334	A	20060222	ZA 2004-9334	20041119
	US 2006105997	A1	20060518	US 2004-517559	20041208
	IN 2004CN02798	A	20060210	IN 2004-CN2798	20041210
	NO 2005000198	A	20050311	NO 2005-198	20050113
PRAI	US 2002-388621P	P	20020614		
	US 2002-403830P	P	20020815		
	US 2002-426940P	P	20021115		
	US 2003-458318P	P	20030328		
	WO 2003-US18482	W	20030612		

OS MARPAT 140:77020

GI



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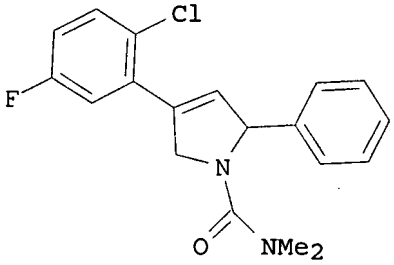


II

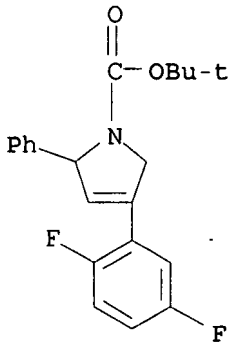
AB The invention relates to dihydropyrrole compds. that are useful for treating cellular proliferative diseases and disorders associated with KSP kinesin activity. The invention also relates to compns. which comprise these compds. and methods of using them to treat cancer in mammals. Compds. I [R1 is (C1-C6-alkylene)n-X-R, (n is 0 or 1; X is CO, SO2, NH, PO, etc.; R is alkyl, aryl, amino group, etc.), aryl, heterocyclyl, or alkyl; R2, R6 are aryl, aralkyl, cycloalkyl, or heterocyclyl; R3-R5, R7-R9 are H, alk(en)(yn)yl, aryl, aralkyl, heterocyclyl, etc.] (including amino acid derivs.) are claimed. For example, a detailed synthesis for the preparation of II is outlined, which includes reaction of 2 chloro-5-fluorobenzenediazonium tetrafluoroborate with Boc-protected 2,5-dihydro-1H-pyrrole-1-carboxylate.

IT 635724-42-4P 635724-48-0P 639072-35-8P
639072-50-7P 639074-72-9P 639075-20-0P
639075-47-1P 639075-53-9P 639077-57-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrrole derivs. as mitotic kinesin inhibitors)

RN 635724-42-4 CAPLUS

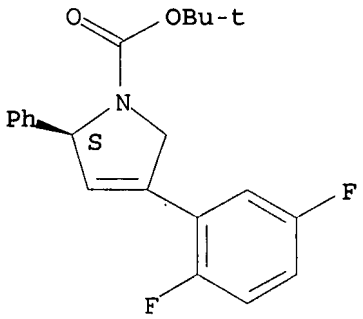
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 635724-48-0 CAPLUS

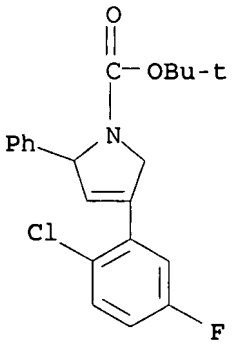
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



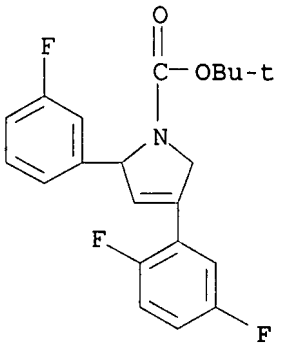
RN 639072-35-8 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 4-(2-chloro-5-fluorophenyl)-2,5-dihydro-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

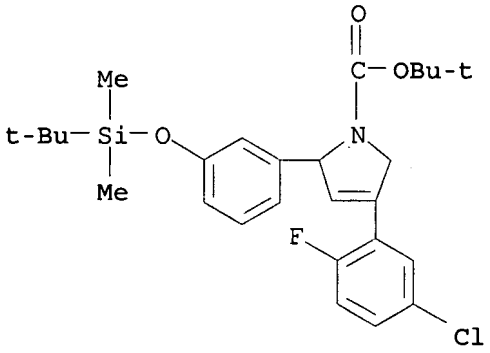


RN 639072-50-7 CAPLUS

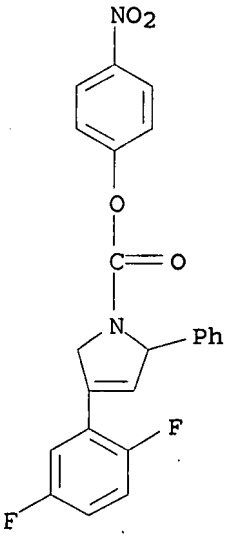
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2-(3-fluorophenyl)-2,5-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



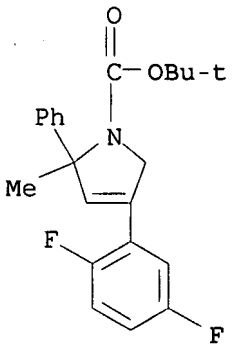
RN 639074-72-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(5-chloro-2-fluorophenyl)-2-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]-2,5-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 639075-20-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-phenyl-, 4-nitrophenyl ester (9CI) (CA INDEX NAME)

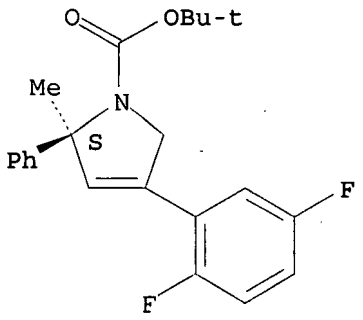


RN 639075-47-1 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-methyl-2-phenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

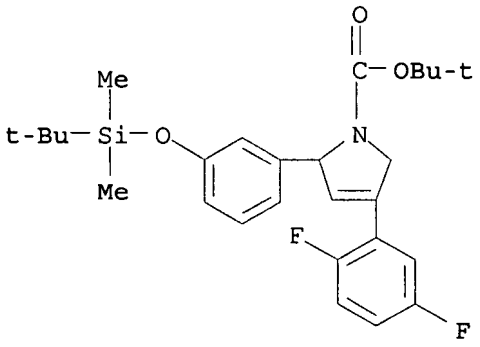


RN 639075-53-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2,5-dihydro-2-methyl-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



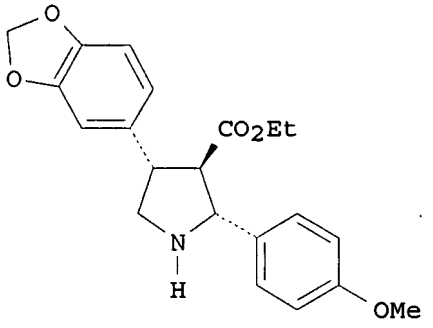
RN 639077-57-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 4-(2,5-difluorophenyl)-2-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]phenyl]-2,5-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:786710 CAPLUS
DN 139:381435
TI Enantioselective synthesis of the pyrrolidine core of endothelin antagonist ABT-627 (Atrasentan) via 1,2-oxazines
AU Buchholz, Monika; Reissig, Hans-Ulrich
CS Institut fuer Chemie - Organische Chemie, Freie Universitaet Berlin,

Berlin, 14195, Germany
SO European Journal of Organic Chemistry (2003), (18), 3524-3533
CODEN: EJOCFK; ISSN: 1434-193X
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 139:381435
GI



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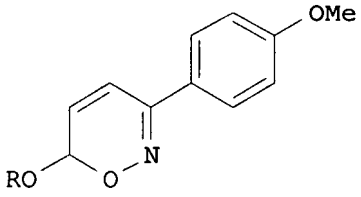


II

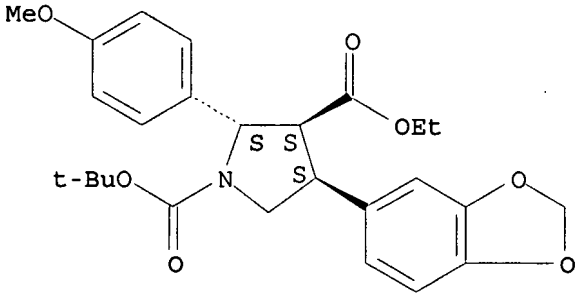
AB Diastereoselective syntheses of the pyrrolidine core I of the endothelin antagonist ABT-627 (Atrasentan) as a racemic mixture and as an enantiopure compound are presented. The crucial steps of these syntheses utilized the highly diastereoselective conjugate addition of 1,3-benzodioxol-5-yl-lithium to racemic 6H-1,2-oxazine II (R = Et) or enantiopure 6H-1,2-oxazines II [R = (+)- or (-)-menthol], followed by trapping with Et cyanoformate (Mander's reagent). The resulting 5,6-dihydro-4H-1,2-oxazines were transformed into the 2,3,4-trisubstituted pyrrolidine I.

IT 624736-81-8P
RL: BYP (Byproduct); PREP (Preparation)
(byproducts from the stereoselective preparation of diarylpyrrolidinecarboxylates via hydrogenation of aryloxazinecarboxylates followed by fragmentation, protection, cyclization, and deprotection)

RN 624736-81-8 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2S,3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



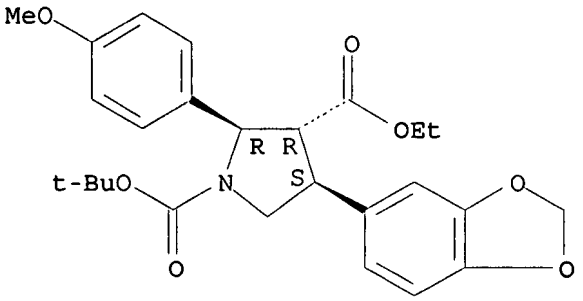
IT 209214-29-9P 624736-69-2P 624736-79-4P
624736-80-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation of diarylpyrrolidinecarboxylates via hydrogenation of aryloxazinecarboxylates followed by fragmentation,

protection, cyclization, and deprotection)

RN 209214-29-9 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

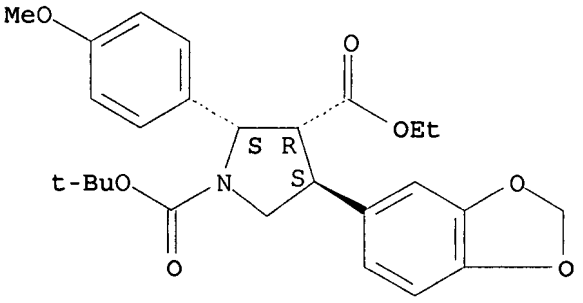
Relative stereochemistry.



RN 624736-69-2 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3S,4R)-rel- (9CI) (CA INDEX NAME)

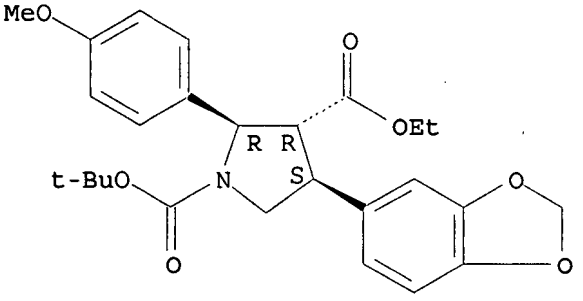
Relative stereochemistry.



RN 624736-79-4 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

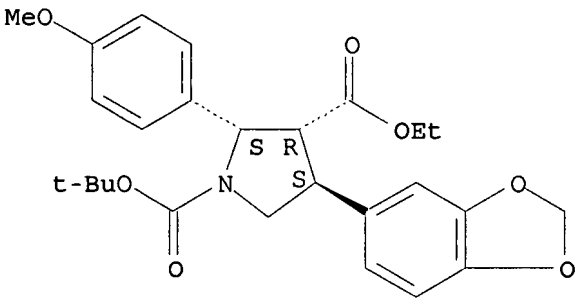


RN 624736-80-7 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2S,3R,4S)- (9CI)

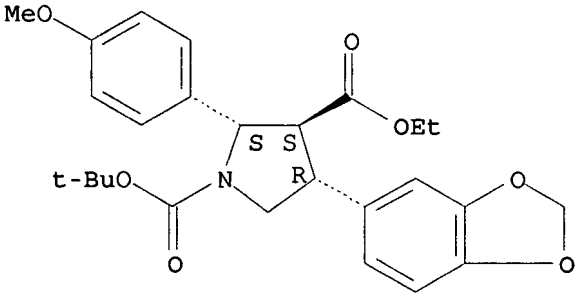
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



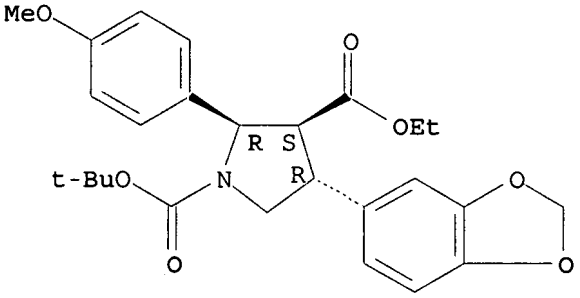
IT 624736-82-9P 624736-83-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of diarylpyrrolidinecarboxylates via hydrogenation of aryloxazinecarboxylates followed by fragmentation, protection, cyclization, and deprotection)
RN 624736-82-9 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2S,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 624736-83-0 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:396850 CAPLUS
DN 138:401597
TI Preparation of arylpyrrolidinones as neurokinin-1 (NK1) antagonists.
IN Reichard, Gregory A.; Paliwal, Sunil; Shih, Neng-Yang; Xiao, Dong; Tsui, Hon-Chung; Shah, Sapna; Wang, Cheng; Wrobleski, Michelle L.
PA Schering Corporation, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003042173	A1	20030522	WO 2002-US36186	20021112
	WO 2003042173	A8	20031002		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2466465	A1	20030522	CA 2002-2466465	20021112
	AU 2002363642	A1	20030526	AU 2002-363642	20021112
	US 2003144270	A1	20030731	US 2002-292618	20021112
	US 7122677	B2	20061017		
	EP 1451153	A1	20040901	EP 2002-803200	20021112
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	CN 1585748	A	20050223	CN 2002-822380	20021112
	JP 2005509031	T	20050407	JP 2003-544010	20021112
PRAI	US 2001-337652P	P	20011113		
	WO 2002-US36186	W	20021112		

OS MARPAT 138:401597
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; Q = (CR6R7)n2; X1 = O, S, SO, SO2, NR18a, N(COR12), N(SO2R15); X2 = C, S, SO; Y = O, S, NR11; R1, R2 = H, alkyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, CH2F, CHF2 CF3; R1R2 = alkylene, CO; R3 = alkyl, hydroxyalkyl, cycloalkyl, CH2F, CHF2, CF3; R4, R5 = (CR28R29)n1G, C(O)(CR28R29)n4G; n1 = 0-5; n2 = 1-4; n4 = 1-5; G = H, CF3, CHF2, CH2F, OH, alkoxy, SO2R13, cycloalkoxy, NR13R14, SO2NR13R14, NR13SO2R15, NR13COR12NR12(CONR13R14), NR12COC(R12)2NR13R14, CONR13R14, COOR12, cycloalkyl, (R19)r-aryl, (R19)r-heteroaryl, O2CR14, O2CNR13R14, etc.; R4R5 = CO, NR12, atoms to form 4-7 membered ring; R6 = H, alkyl, OR13, SR18; R7 = H, alkyl; R6R7 = CO; R12 = H, alkyl, cycloalkyl, cycloalkylalkyl; R13, R14 = H, alkyl, cycloalkyl, cycloalkylalkyl; R13R14 = atoms to form 4-7 membered ring; R18 = H, alkyl, cycloalkyl, cycloalkylalkyl, P(O)(OH)2; R18a = H, alkyl, cycloalkyl, cycloalkylalkyl; Ar1, Ar2 = (substituted) Ph, heteroaryl; R28, R29 = H, alkyl, CH2F, CHF2, CF3; with provisos], were prepared as NK1 antagonists (no data). Thus, aminoamide (II) was autoclaved with Ba(OH)2 in H2O at 155° followed by treatment (Boc)2O to give 96% Boc-protected acid. The latter in CH2Cl2 was treated with triphosgene and diisopropylethylamine to give 94% cyclic anhydride, which was condensed with EtOAc using LDA in THF to give 88% acetoacetate derivative,

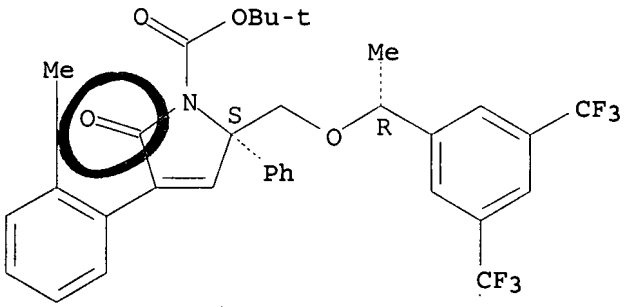
which in CH2Cl2 was treated with HCl in dioxane to give title compound (III).

IT 530454-84-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of arylpyrrolidinones as NK1 antagonists)

RN 530454-84-3 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2-[[(1R)-1-[3,5-bis(trifluoromethyl)phenyl]ethoxy]methyl]-2,5-dihydro-4-(2-methylphenyl)-5-oxo-2-phenyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L111 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:171682 CAPLUS

DN 136:232311

TI Preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivatives as endothelin antagonists

IN Winn, Martin; Boyd, Steven A.; Hutchins, Charles W.; Hwan-Soo, Jae; Tasker, Andrew S.; Von Geldern, Tomas W.; Kester, Jeffrey; Sorensen, Bryan K.; Szczepankiewicz, Bruce G.; Henry, Kenneth; Liu, Gang; Wittenberger, Steven J.; King, Steven A.; Janus, Todd J.; Padley, Robert J.

PA Abbott Laboratories, USA

SO PCT Int. Appl., 817 pp.
CODEN: PIXXD2

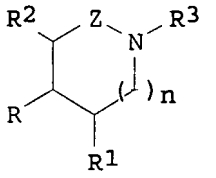
DT Patent

LA English

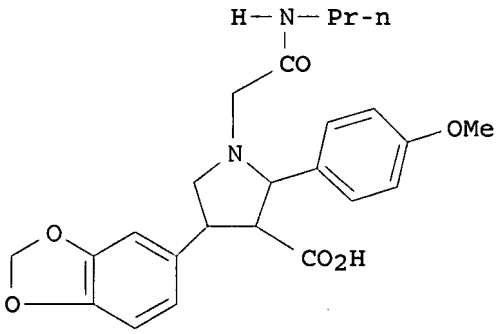
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002017912	A1	20020307	WO 2001-US27220	20010831
	W: CA, JP, MX				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	US 7208517	B1	20070424	US 2000-653563	20000831
	AU 200227636	A	20020516	AU 2002-27636	20020325
	AU 2005201160	A1	20050414	AU 2005-201160	20050317
PRAI	US 2000-653563	A	20000831		
	US 1994-293349	B2	19940819		
	US 1994-334717	B2	19941104		
	US 1995-442575	A2	19950530		
	US 1995-497998	B2	19950802		
	US 1996-600625	B2	19960213		
	US 1997-794506	B2	19970204		
	US 1998-48955	B2	19980327		
	AU 1998-85921	A3	19980727		
	US 2000-634661	B2	20000807		
	AU 2002-27636	A3	20020325		

OS MARPAT 136:232311
GI



I



II

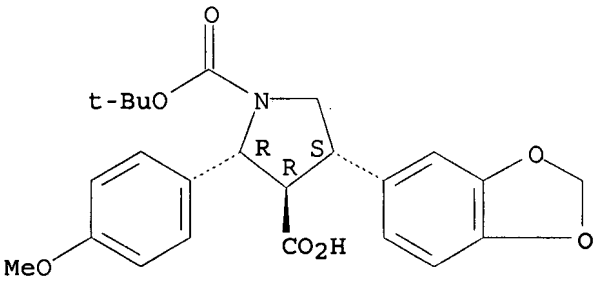
AB Title compds. [I; n = 0; Z = CH2; R = CO2H; R1 = alkoxyaryl, alkoxyalkoxyaryl, heterocyclylalkyl; R2 = 1,3-benzodioxyl, 4-benzofuranyl, 5-indanyl; R3 = R4R5CO; R4 = R6R7N, R8R9NNH; R5 = methylene; one of R6, R7 is H, the other is arylalkyl, diarylalkyl; one of R8, R9 is alkyl, the other is aryl] stereoisomers, and pharmaceutically acceptable salts are prepared as endothelin antagonists. Thus, the title compound II was prepared from Et (4-methoxybenzoyl)acetate, 5-(2-nitrovinyl)-1,3-benzodioxol, ethyldiisopropylamine, and N-Pr bromoacetamide and was in vitro tested for binding effect to the endothelin receptor and the determination of title compound as functional ET antagonist.

IT 173864-48-7P 209214-29-9P 209214-30-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

RN 173864-48-7 CAPLUS

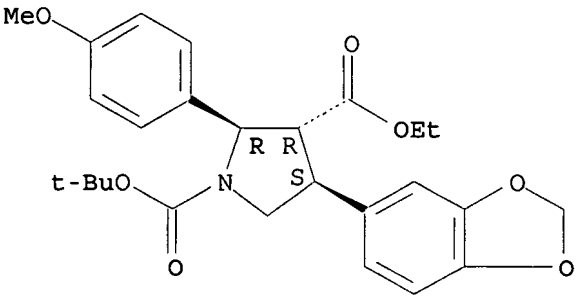
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



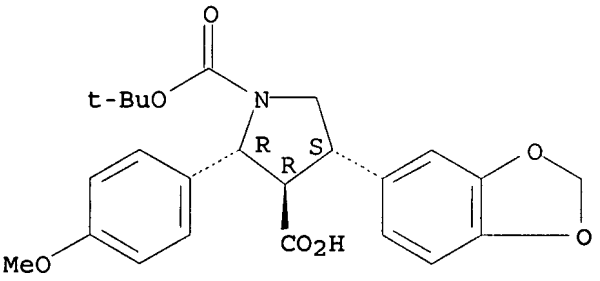
RN 209214-29-9 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 209214-30-2 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester, (2R,3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

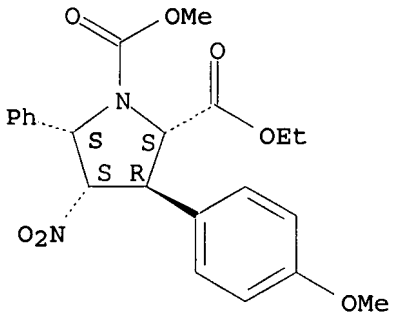


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:812647 CAPLUS
DN 134:100728
TI A new synthesis of 3,5-diarylpyrrole-2-carboxylic acids and esters
AU Fejes, Imre; Toke, Laszlo; Blasko, Gabor; Nyerges, Miklos; Pak, Chwang Siek
CS Research Group of the Hungarian Academy of Sciences, Department of Organic Chemical Technology, Technical University of Budapest, Budapest, H-1521, Hung.
SO Tetrahedron (2000), 56(43), 8545-8553

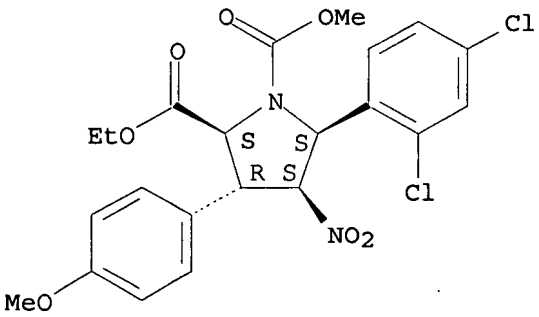
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 134:100728
AB A new two-step synthesis of pyrrole-2-carboxylic acids via 1,3-dipolar cycloaddn. of azomethine ylides to nitrostyrenes and oxidation of the resulting pyrrolidines with alkaline hydrogen peroxide is described. The oxidation of the cycloadducts by MnO2 under different conditions also has been examined
IT 245090-32-8P 320349-64-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3,5-diarylpyrrole-2-carboxylic acids and esters)
RN 245090-32-8 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-(4-methoxyphenyl)-4-nitro-5-phenyl-, 2-ethyl 1-methyl ester, (2R,3S,4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



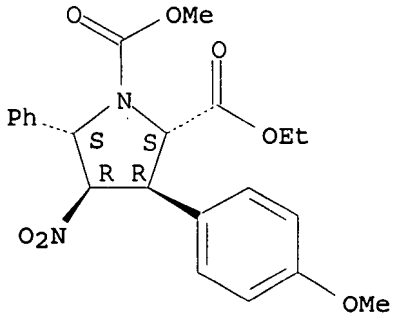
RN 320349-64-2 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 5-(2,4-dichlorophenyl)-3-(4-methoxyphenyl)-4-nitro-, 2-ethyl 1-methyl ester, (2R,3S,4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



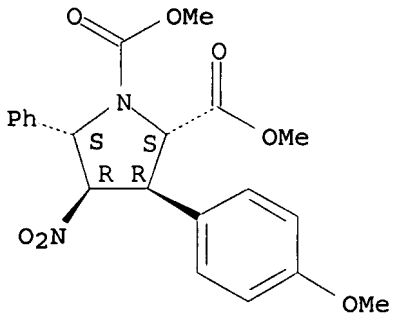
IT 245090-33-9P 320349-65-3P 320349-66-4P
320349-67-5P 320349-68-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of 3,5-diarylpyrrole-2-carboxylic acids and esters)
RN 245090-33-9 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-(4-methoxyphenyl)-4-nitro-5-phenyl-, 2-ethyl 1-methyl ester, (2R,3S,4S,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



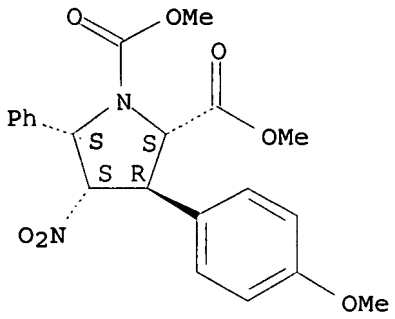
RN 320349-65-3 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-(4-methoxyphenyl)-4-nitro-5-phenyl-, dimethyl ester, (2R,3S,4S,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



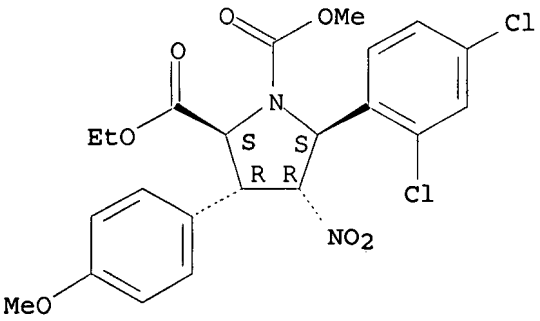
RN 320349-66-4 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-(4-methoxyphenyl)-4-nitro-5-phenyl-, dimethyl ester, (2R,3S,4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



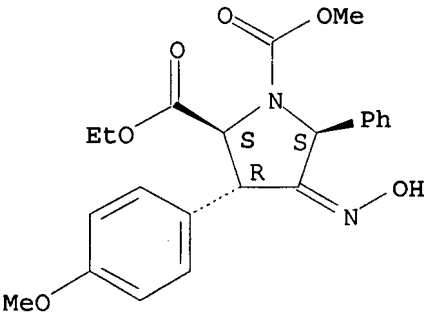
RN 320349-67-5 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 5-(2,4-dichlorophenyl)-3-(4-methoxyphenyl)-4-nitro-, 2-ethyl 1-methyl ester, (2R,3S,4S,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 320349-68-6 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 4-(hydroxyimino)-3-(4-methoxyphenyl)-5-phenyl-, 2-ethyl 1-methyl ester, (2R,3S,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.

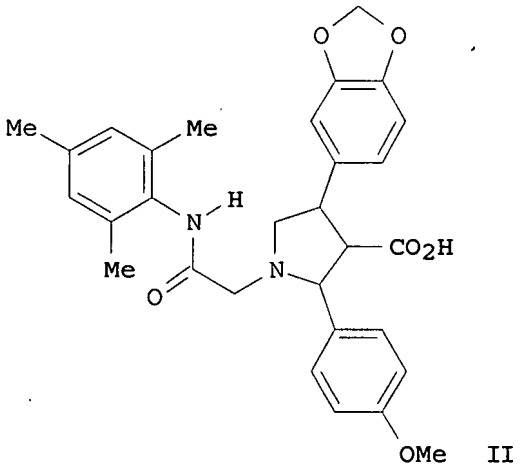


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:687965 CAPLUS
DN 133:252300
TI Preparation of pyrrolidinecarboxylates as endothelin ETB receptor antagonists
IN Tasker, Andrew S.; Winn, Martin; Boyd, Steven A.; Jae, Hwan-Soo; Von Geldern, Thomas W.; Sorensen, Bryan K.; Henry, Kenneth J.
PA Abbott Laboratories, USA
SO U.S., 146 pp., Cont.-in-part of U.S. Ser. No. 877,187.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6124341	A	20000926	US 1998-87178	19980529
	CN 1215401	A	19990428	CN 1997-193633	19970210
	CN 1079397	B	20020220		
	PT 888340	T	20021231	PT 1997-905897	19970210
	ES 2182029	T3	20030301	ES 1997-905897	19970210
	TW 502018	B	20020911	TW 1997-86103700	19970324
	CA 2292604	A1	19981223	CA 1998-2292604	19980608
	BR 9810031	A	20000912	BR 1998-10031	19980608
	MX 9912052	A	20000630	MX 1999-12052	19991217
PRAI	US 1996-600724	B2	19960213		
	US 1997-794505	B2	19970204		
	US 1997-877187	A2	19970617		
	US 1998-87178	A	19980529		

WO 1998-US11821 W 19980608
OS MARPAT 133:252300
GI



II

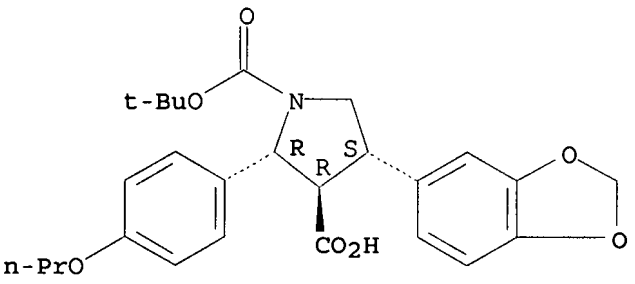
AB R3Z(CH2)mR [I; R = (un)protected CO2H, cyano, alkylcarbamoyl, tetrazolyl, etc.; R3 = Z1CONHR4 or Z2SO2NHR6; R4,R6 = otherwise (un)substituted Ph having halo, (halo)alkyl, cyano, alkoxy, or Ph substituents an the 2- and 6-positions; Z = 2- and/or 4-(un)substituted pyrrolidine-1,3-diyl; Z1,Z2 = bond, (imino)alk(en)ylene, etc.; m = 0-6] were prepared Thus, 4-(MeO)C6H4COCH2CO2Et was alkylated by 5-(2-nitrovinyl)-1,3-benzodioxole (preparation given) and the product reductively cyclized to give, after NaBH3CN reduction, 4-(MeO)C6H4Z3CO2Et [Z3 = 4-(1,3-benzodioxol-5-yl)pyrrolidine-2,3-diyl] as a mixture of trans,trans and cis,trans isomers which was N-alkylated by BrCH2CONHC6H2Et3-2,4,6 to give, after saponification, title compound trans,trans-II. Data for biol. activity of I were given.

IT 195529-66-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolidinecarboxylates as endothelin ETB receptor antagonists)

RN 195529-66-9 CAPLUS

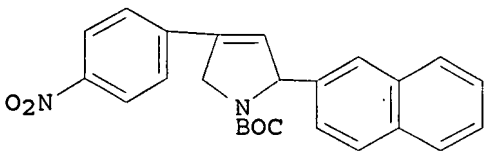
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-propoxyphenyl)-, 1-(1,1-dimethylethyl) ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



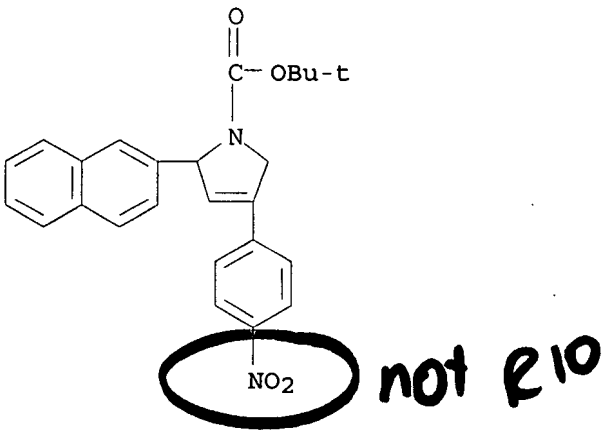
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:521087 CAPLUS
DN 133:252243
TI Heck arylation of N-Boc-3-pyrrolines and N-Boc-2-pyrrolines with diazonium salts; efficient syntheses of five-membered 4-aryl endocyclic enecarbamates and N-Boc-2,4-diaryl 3-pyrrolines
AU Carpes, Marcos Jose S.; Correia, Carlos Roque D.
CS Instituto de Quimica, UNICAMP, Sao Paulo, 13083-970, Brazil
SO Synlett (2000), (7), 1037-1039
CODEN: SYNLES; ISSN: 0936-5214
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 133:252243
GI



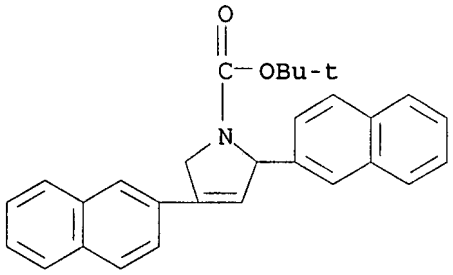
I

AB Practical and efficient Heck arylations of N-Boc-3-pyrrolines and N-Boc-4-aryl-2-pyrrolines (endocyclic enecarbamates) with several arenediazonium tetrafluoroborate salts were accomplished. This methodol. permitted the preparation of a series of 4-aryl endocyclic enecarbamates which were used in a subsequent Heck arylation to produce biaryl-3-pyrrolines, e.g. I, in good yields without the need for phosphine ligands, excess of olefin, and stringent reaction conditions.
IT 295357-61-8P 295357-63-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(efficient preparation of five-membered 4-aryl endocyclic enecarbamates and N-Boc-2,4-diaryl-3-pyrrolines via Heck arylation)
RN 295357-61-8 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,5-dihydro-2-(2-naphthalenyl)-4-(4-nitrophenyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



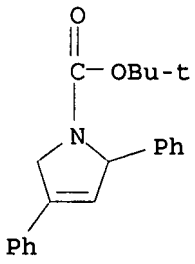
not R10

RN 295357-63-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,5-dihydro-2,4-di-2-naphthalenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:777606 CAPLUS
DN 132:166085
TI Ring-closing metathesis of phenyl-substituted dienes
AU Bujard, M.; Briot, A.; Gouverneur, V.; Mioskowski, C.
CS Laboratoire de Synthese Bio-Organique, CNRS et Universite Louis Pasteur, Faculte de Pharmacie, Illkirch-Graffenstaden, 67401, Fr.
SO Tetrahedron Letters (1999), 40(50), 8785-8788
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 132:166085
AB A series of phenyl-substituted heterodienes, CH2:CPhCH2XCRR1CR2:CH2 [X = NHCO2CMe3 with R = R1 = R2 = H, R = Ph, R1 = R2 = H; R = PhCH2, R1 = R2 = H; R = PhCH2O(CH2)5, R1 = R2 = H; R = Me, R1 = Ph, R2 = H; R = R1 = H, R2 = Me or X = O, R = R1 = R2 = H], was prepared and subjected to ring-closure metathesis (RCM) to give differently phenyl-substituted dihydropyrroles and dihydrofuran.
IT 256950-62-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn of hydropyrroles and hydrofuran by ring-closure metathesis of Ph heterodienes)
RN 256950-62-6 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,5-dihydro-2,4-diphenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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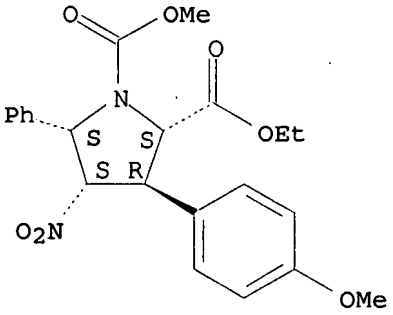
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:516279 CAPLUS
DN 131:257402
TI A new synthesis of pyrrole-2-carboxylic acids
AU Pak, Chwang Siek; Nyerges, Miklos
CS Korea Research Institute Chemical Technology, Taejon, 305606, S. Korea
SO Synlett (1999), (8), 1271-1273

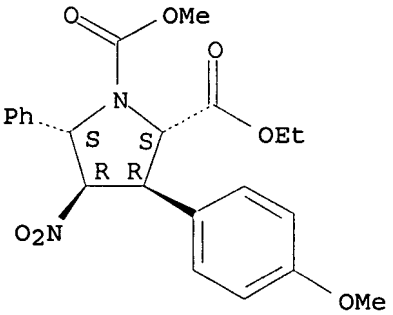
CODEN: SYNLES; ISSN: 0936-5214
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 131:257402
AB The 2-step synthesis of pyrrole-2-carboxylates, via 1,3-dipolar cycloaddn. of azomethine ylides to nitrostyrenes and oxidation of the resulting pyrrolidines with alkaline H2O2, is described.
IT 245090-32-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolecarboxylates)
RN 245090-32-8 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-(4-methoxyphenyl)-4-nitro-5-phenyl-, 2-ethyl 1-methyl ester, (2R,3S,4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 245090-33-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyrrolecarboxylates)
RN 245090-33-9 CAPLUS
CN 1,2-Pyrrolidinedicarboxylic acid, 3-(4-methoxyphenyl)-4-nitro-5-phenyl-, 2-ethyl 1-methyl ester, (2R,3S,4S,5R)-rel- (9CI) (CA INDEX NAME)

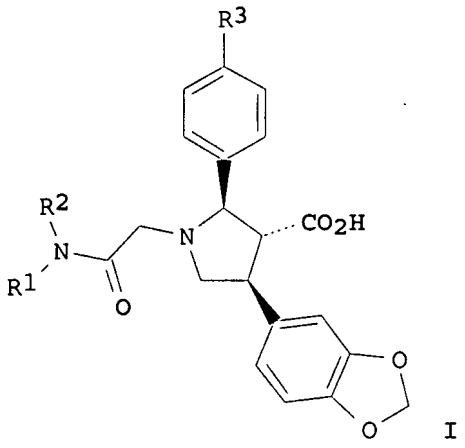
Relative stereochemistry.



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:510837 CAPLUS
DN 131:286357
TI Design, Synthesis, and Activity of a Series of Pyrrolidine-3-carboxylic Acid-Based, Highly Specific, Orally Active ETB Antagonists Containing a Diphenylmethylamine Acetamide Side Chain
AU Liu, Gang; Kozmina, Natasha S.; Winn, Martin; von Geldern, Thomas W.; Chiou, William J.; Dixon, Douglas B.; Nguyen, Bach; Marsh, Kennan C.;

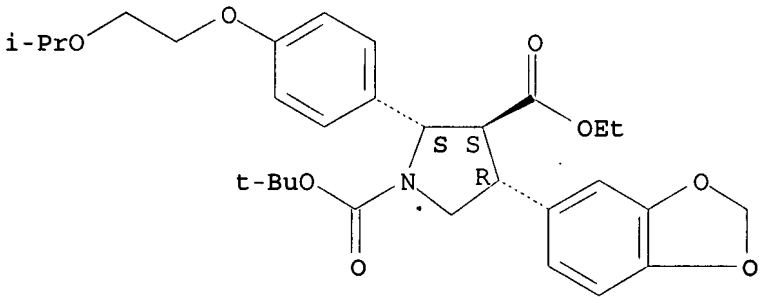
Opgenorth, Terry J.
CS Metabolic Disease Research and Drug Analysis Department Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, 60064-6098, USA
SO Journal of Medicinal Chemistry (1999), 42(18), 3679-3689
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I

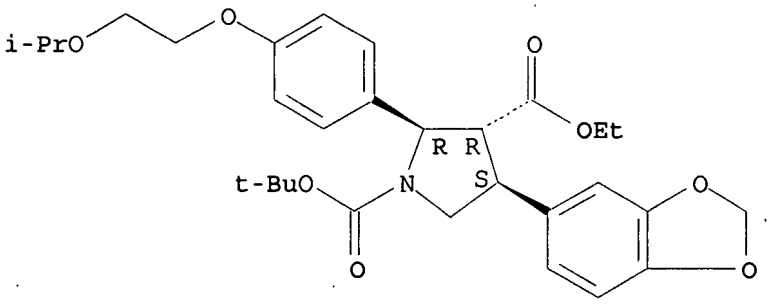
AB The endothelin (ET)-B receptor subtype is expressed on vascular endothelial and smooth muscle cells and mediates both vasodilation and vasoconstriction. On the basis of the pharmacophore of the previously reported ETA-specific antagonist I (R1 = R2 = n-Bu; R3 = MeO)(ABT-627), we are reporting the discovery of a novel series of highly specific, orally active ETB receptor antagonists. Replacing the dibutylaminoacetamide group of I with a diphenylmethylaminoacetamide group resulted in antagonist I (R1 = (C6H5)2CH; R2 = H; R3 = MeO) with a complete reversal of receptor specificity. Structure-activity relationship studies revealed that ortho-alkylation of the Ph rings could further increase ETB affinity and also boost the ETA/ETB activity ratio of the resulting antagonists. A similar antagonism selectivity profile could also be achieved when one of the Ph rings of the acetamide side chain was replaced with an alkyl group, preferably a tert-Bu group I [R1 = C6H5(t-Bu)CH; R2 = H; R3 = MeO]. Combining these features with modification of the 2-aryl group of the pyrrolidine core, we have identified a potent antagonist I [R1 = (2-MeC6H4)2CH; R2 = H; R3 = MeOCH2CH2O](A-308165) with over 27 000-fold selectivity favoring the ETB receptor and an acceptable pharmacokinetic profile (F = 24%) in rats.
IT 246853-50-9P
RL: PUR (Purification or recovery); PREP (Preparation)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
RN 246853-50-9 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2S,3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



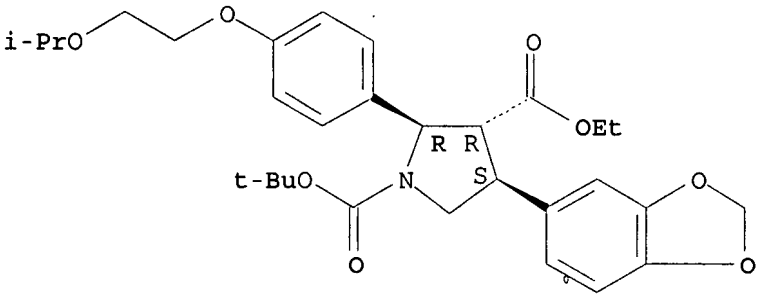
IT 246853-51-0P
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
RN 246853-51-0 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 246853-49-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
RN 246853-49-6 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

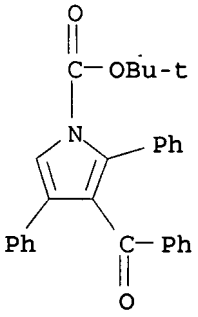
Relative stereochemistry.



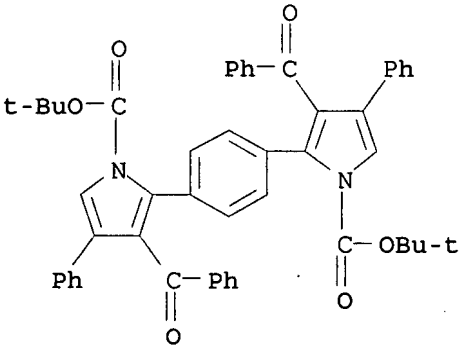
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:173742 CAPLUS
DN 131:5312
TI A Direct Synthesis of 2-(Trimethylstannyl)pyrroles from Michael Acceptors and Stannylated Tosylmethyl Isocyanide. [Erratum to document cited in CA129:189411]
AU Dijkstra, Harm P.; ten Have, Ronald; Van Leusen, Albert M.
CS Dep. Organic Molecular Inorganic Chem., Groningen Univ., Groningen, 9747 AG, Neth.
SO Journal of Organic Chemistry (1999), 64(7), 2599
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
AB The claim that "stannylated pyrroles with a free N-H function have not been reported previously" appears to be incorrect. Two such compds. [5-(tri-n-butylstannyl)pyrrole-2-carbaldehyde (Denat et al., 1992; Veith et al., 1993) and 4-(trimethylstannyl)pyrrole-2-carbaldehyde (Veith et al., 1993)] have been reported by Dubac et al. The latter compds., furthermore, is a second example of a 3-stannylpyrrole.
IT 211741-71-8P 211741-73-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (trimethylstannyl)pyrroles from Michael acceptors and stannylated tosylmethyl isocyanide (Erratum))
RN 211741-71-8 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 3-benzoyl-2,4-diphenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 211741-73-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,2'-(1,4-phenylene)bis[3-benzoyl-4-phenyl-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L11 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:113673 CAPLUS
DN 130:182352
TI Preparation of substituted pyrrolidine-3-carboxylic acids as endothelin antagonists
IN Winn, Martin; Boyd, Steven A.; Hutchins, Charles W.; Jae, Hwan-Soo; Tasker, Andrew S.; Von Geldern, Thomas W.; Kester, Jeffrey A.; Sorensen, Bryan K.; Szczepankiewicz, Bruce G.; Henry, Kenneth J.; Liu, Gang; Wittenberger, Steven J.; King, Steven A.
PA Abbott Laboratories, USA
SO PCT Int. Appl., 821 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9906397	A2	19990211	WO 1998-US15479	19980727
	WO 9906397	A3	19991209		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6162927	A	20001219	US 1997-905913	19970804
	CA 2297894	A1	19990211	CA 1998-2297894	19980727
	AU 9885921	A	19990222	AU 1998-85921	19980727
	AU 748469	B2	20020606		
	EP 1003740	A2	20000531	EP 1998-937139	19980727
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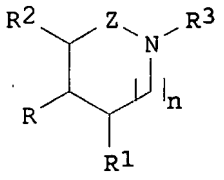
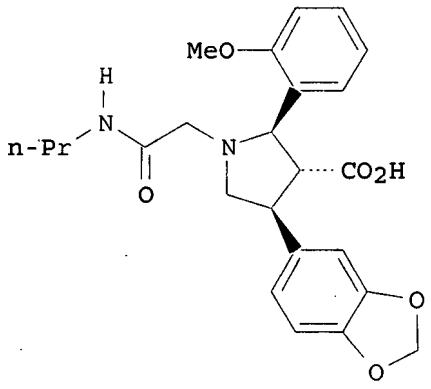
	JP 2001512119	T	20010821	JP 2000-505155	19980727
	BR 9815296	A	20011120	BR 1998-15296	19980727
	HU 200003484	A2	20020128	HU 2000-3484	19980727
	NZ 502395	A	20020828	NZ 1998-502395	19980727
	NO 2000000542	A	20000404	NO 2000-542	20000202
	MX 200001283	A	20001030	MX 2000-1283	20000204
	BG 104216	A	20001229	BG 2000-104216	20000302
	AU 200227636	A	20020516	AU 2002-27636	20020325
	AU 2005201160	A1	20050414	AU 2005-201160	20050317
PRAI	US 1997-905913	A	19970804		
	US 1998-48955	A	19980327		
	US 1994-293349	B2	19940819		
	US 1994-334717	B2	19941104		
	US 1995-442575	A2	19950530		
	US 1995-497998	B2	19950802		
	US 1996-600625	B2	19960213		
	US 1997-794506	A2	19970204		
	AU 1998-85921	A3	19980727		
	WO 1998-US15479	W	19980727		
	AU 2002-27636	A3	20020325		

OS MARPAT 130:182352
GI



I



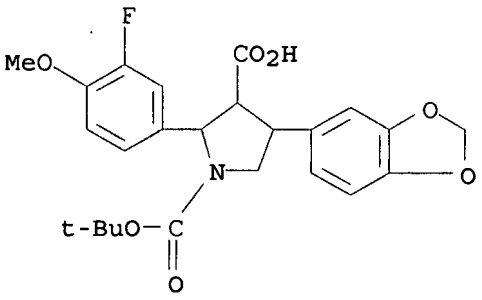
II

AB The title compds. [I; Z = CR18R19, C(O) (wherein R18, R19 = H, lower alkyl); n = 0-1; R = CN, OH, alkoxy, etc.; R1, R2 = H, lower alkyl, alkenyl, etc.; R3 = R4C(O)R5-, R4R5a-, R4C(O)R5NR6- (wherein R5 = a bond, alkylene, alkenylene, etc.; R5a = alkylene, alkenylene; R4, R6 = H, lower alkyl, haloalkyl, etc.), etc.], useful in treatment of conditions such as hypertension, congestive heart failure, atherosclerosis, etc., were prepared and formulated. E.g., a 4-step synthesis of the title compound trans,trans-II which showed 96.4% inhibition of ETA at 1 μM, was given.

IT 220584-77-0P 220584-78-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted pyrrolidine-3-carboxylic acids as endothelin antagonists)

RN 220584-77-0 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(3-fluoro-4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

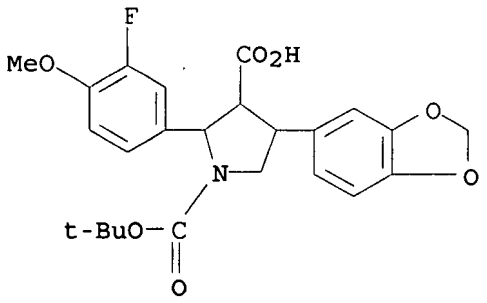


RN 220584-78-1 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(3-fluoro-4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester, compd. with (αS)-α-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

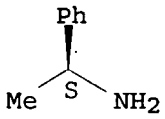
CRN 220584-77-0
CMF C24 H26 F N O7



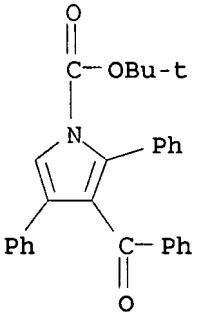
CM 2

CRN 2627-86-3
CMF C8 H11 N

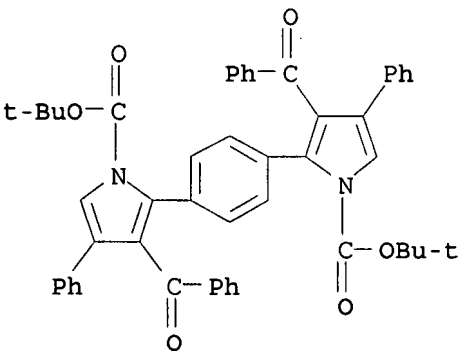
Absolute stereochemistry. Rotation (-).



L11 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:496397 CAPLUS
DN 129:189411
TI A Direct Synthesis of 2-(Trimethylstannyl)pyrroles from Michael Acceptors and Stannylated Tosylmethyl Isocyanide
AU Dijkstra, Harm P.; ten Have, Ronald; van Leusen, Albert M.
CS Department of Organic and Molecular Inorganic Chemistry, Groningen University, Groningen, 9747 AG, Neth.
SO Journal of Organic Chemistry (1998), 63(16), 5332-5338
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
AB 2-(Trimethylstannyl)pyrroles (3), with substituents at the 3- and 4-positions, were synthesized efficiently by a base-induced reaction of stannylated TosMIC with Michael acceptors. Stille cross-couplings with bromobenzene and double cross-couplings with 1,4-dibromobenzene were achieved successfully with the N-Me derivative and the N-Boc derivative of 3-benzoyl-2-(trimethylstannyl)-4-phenylpyrrole (3a), despite the bulk of these stannylpyrroles. Homo-coupling reactions of the same stannylpyrroles with the corresponding bromopyrroles (prepared from stannylpyrroles 3 and NBS) were unsuccessful, probably for steric reasons.
IT 211741-71-8P 211741-73-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (trimethylstannyl)pyrroles from Michael acceptors and stannylated tosylmethyl isocyanide)
RN 211741-71-8 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 3-benzoyl-2,4-diphenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 211741-73-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,2'-(1,4-phenylene)bis[3-benzoyl-4-phenyl-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

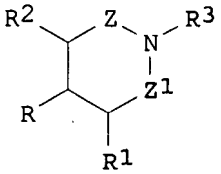
L11 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:414738 CAPLUS
DN 129:95396
TI Preparation of 1-(carbamoylmethyl)pyrrolidine-3-carboxylates and analogs as endothelin antagonists
IN Winn, Martin; Boyd, Steven A.; Hutchins, Charles W.; Jae, Hwan-Soo; Tasker, Andrew S.; Von Geldern, Thomas W.; Kester, Jeffrey A.; Sorensen, Bryan K.
PA Abbott Laboratories, USA
SO U.S., 109 pp., Cont.-in-part of U.S. Ser. No. 334,717, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5767144	A	19980616	US 1995-442575	19950530
	US 5622971	A	19970422	US 1995-457935	19950601
	US 5731434	A	19980324	US 1995-458094	19950601
	CA 2195677	A1	19960229	CA 1995-2195677	19950804
	CA 2195677	C	20051108		
	CA 2517691	A1	19960229	CA 1995-2517691	19950804
	WO 9606095	A1	19960229	WO 1995-US9924	19950804
	W: AU, CA, JP, KR, MX				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9532137	A	19960314	AU 1995-32137	19950804
	AU 711832	B2	19991021		
	EP 776324	A1	19970604	EP 1995-928323	19950804

	EP 776324	B1	20020612		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 10504565	T	19980506	JP 1996-508101	19950804
	JP 3741441	B2	20060201		
	EP 1186603	A2	20020313	EP 2001-125462	19950804
	EP 1186603	A3	20030709		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
	AT 219077	T	20020615	AT 1995-928323	19950804
	PT 776324	T	20021129	PT 1995-928323	19950804
	ES 2179881	T3	20030201	ES 1995-928323	19950804
	IL 114894	A	20030410	IL 1995-114894	19950810
	NZ 514171	A	20031031	NZ 1997-514171	19970212
	US 6162927	A	20001219	US 1997-905913	19970804
	HK 1008328	A1	20030207	HK 1998-109192	19980715
	AU 9920344	A	19990603	AU 1999-20344	19990310
	AU 725122	B2	20001005		
	US 6462194	B1	20021008	US 2000-572493	20000515
	US 7208517	B1	20070424	US 2000-653563	20000831
	US 6380241	B1	20020430	US 2000-714934	20001117
	AU 200227636	A	20020516	AU 2002-27636	20020325
	US 6946481	B1	20050920	US 2002-266270	20021008
	US 2006229280	A1	20061012	US 2005-63476	20050223
	AU 2005201160	A1	20050414	AU 2005-201160	20050317
PRAI	US 1994-293349	B2	19940819		
	US 1994-334717	B2	19941104		
	US 1995-442575	B3	19950530		
	US 1995-497998	A	19950802		
	AU 1995-32137	A3	19950804		
	CA 1995-2195677	A3	19950804		
	EP 1995-928323	A3	19950804		
	WO 1995-US9924	W	19950804		
	US 1996-600625	B2	19960213		
	US 1997-794506	A2	19970204		
	NZ 1997-503365	A1	19970212		
	US 1997-905913	A3	19970804		
	US 1998-48955	B2	19980327		
	AU 1998-85921	A3	19980727		
	US 2000-572493	A1	20000515		
	US 2000-634661	B2	20000807		
	AU 2002-27636	A3	20020325		
	US 2002-266270	A1	20021008		

OS MARPAT 129:95396

GI



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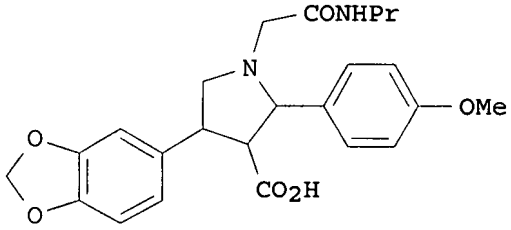


II

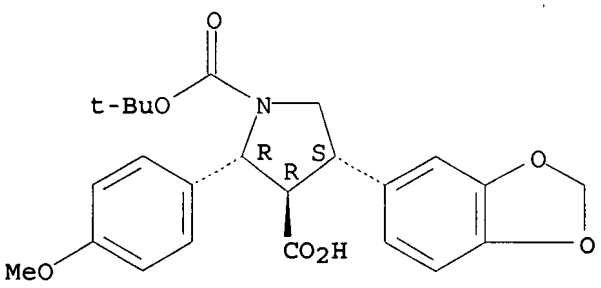
AB Title compds. [I; R = (CH2)mR4; R1,R2 = H, (un)substituted alkyl, heterocyclyl, aryl, etc.; R3 = acyl(alkyl), etc.; R4 = OH, alkoxy, acyl, heterocyclyl, etc.; Z = CH2, CO, alkylidene; Z1 = bond or CH2; m = 0-6] were prepared Thus, 4-(MeO)C6H4COCH2CO2Et was alkylated by 5-(2-nitrovinyl)-1,3-benzodioxole and the product reductively cyclized to give, in 3 addnl. steps, title compound II. Data for biol. activity of I

were given.

IT 173864-48-7P 209214-29-9P 209214-30-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-(carbamoylmethyl)pyrrolidine-3-carboxylates and analogs as endothelin antagonists)

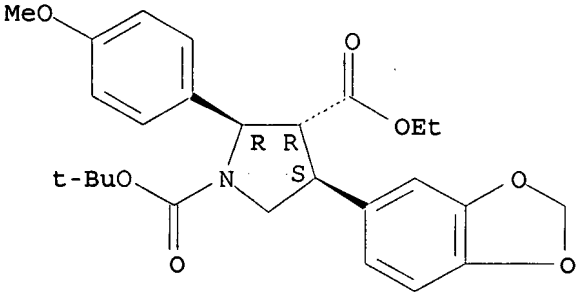
RN 173864-48-7 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



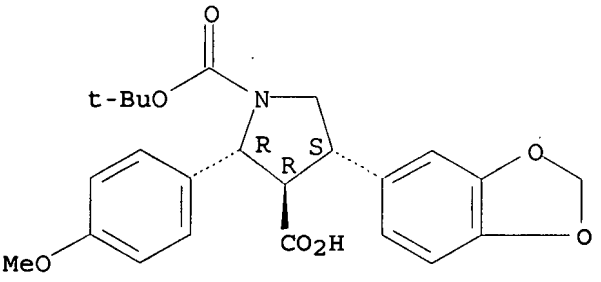
RN 209214-29-9 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) 3-ethyl ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 209214-30-2 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester, (2R,3R,4S)- (9CI) (CA INDEX NAME)

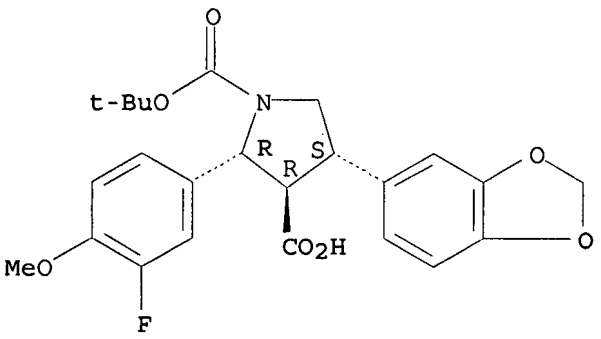
Absolute stereochemistry. Rotation (+).



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:603434 CAPLUS
DN 127:242813
TI Pyrrolidine-3-carboxylic Acids as Endothelin Antagonists. 2. Sulfonamide-Based ETA/ETB Mixed Antagonists
AU Jae, Hwan-Soo; Winn, Martin; Dixon, Douglas B.; Marsh, Kennan C.; Nguyen, Bach; Opgenorth, Terry J.; von Geldern, Thomas W.
CS Metabolic Diseases Research and Drug Analysis Department Pharmaceutical Products Research Division, Abbott Laboratories, Abbott Park, IL, 60064, USA
SO Journal of Medicinal Chemistry (1997), 40(20), 3217-3227
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB When the N,N-dialkylacetamide side chain of the highly ETA-selective endothelin antagonist ABT-627 ([2R,3R,4S]-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)-1-[[(N,N-dibutylamino)carbonyl]methyl]pyrrolidine-3-carboxylic acid; A-147627) is replaced by N,S-dialkylsulfonamidoethyl, the resultant analogs retain ETA affinity, but exhibit substantial ETB affinity as well. Structure-activity studies reveal that modifications in the length of the two alkyl groups, and in the substitution on the anisyl ring, are important in optimizing this "balanced" antagonist profile. In particular the combination of an N-Pr group, an S-alkyl chain between four and six carbons in length, and a fluorine atom ortho to the aromatic OCH3 provides compds. with sub-nanomolar affinities for both receptor subtypes, and with ETA/ETB ratios close to 1. A number of these compds. also exhibit oral bioavailabilities (in rats) in the 30-50% range and have substantial plasma half-lives. The balanced receptor-binding profile of these potent and orally bioavailable compds. complements the ETA selectivity observed with ABT-627.
IT 195510-84-0P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation and structure-activity relations of pyrrolidinecarboxylic acids as endothelin antagonists)
RN 195510-84-0 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(3-fluoro-4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester, [2R-(2α,3β,4α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

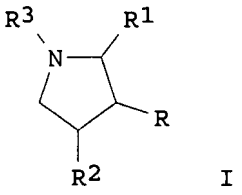


RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:568107 CAPLUS
DN 127:248100
TI Preparation of 4-benzodioxolylpyrrolidine-3-carboxylates and analogs as endothelin receptor antagonists
IN Tasker, Andrew S.; Boyd, Steven A.; Sorensen, Bryan K.; Winn, Martin; Jae, Hwan-soo; Von Geldern, Thomas W.; Henry, Kenneth J.
PA Abbott Laboratories, USA
SO PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9730046	A1	19970821	WO 1997-US2128	19970210
	W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2245684	A1	19970821	CA 1997-2245684	19970210
	AU 9722678	A	19970902	AU 1997-22678	19970210
	AU 714597	B2	20000106		
	EP 888340	A1	19990107	EP 1997-905897	19970210
	EP 888340	B1	20020717		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	BR 9707394	A	19990406	BR 1997-7394	19970210
	HU 9902316	A2	19991129	HU 1999-2316	19970210
	JP 2000504727	T	20000418	JP 1997-529436	19970210
	NZ 331124	A	20000526	NZ 1997-331124	19970210
	NZ 503383	A	20020201	NZ 1997-503383	19970210
	AT 220673	T	20020815	AT 1997-905897	19970210
	ZA 9701184	A	19970827	ZA 1997-1184	19970212
	HK 1019328	A1	20030523	HK 1999-102900	19990707
PRAI	US 1996-600724	A	19960213		
	US 1997-794505	A	19970204		
	WO 1997-US2128	W	19970210		

OS MARPAT 127:248100
GI



I

AB Title compds. [I; R = (CH2)mR5; R1,R2 = H, (un)substituted alkyl, heterocyclyl, aryl, etc.; R3 = Z1COR4 or Z2SO2R6; R4,R6 = (un)substituted 2,6-dialkylphenylamino etc.; R5 = CO2H, OH, cyano, (di)alkylcarbamoyl, etc.; Z1,Z2 = bond, alk(en)ylene, (alkyl)iminoalkylene, etc.; m = 0-6] were prepared Thus, 4-(MeO)C6H4COCH2CO2Et was alkylated by 5-(2-nitrovinyl)-1,3-benzodioxole (preparation each given) and the product reductively cyclized to give, after further reduction, trans,trans-I [R1 = C6H4(OMe)-4, R2 = 1,3-benzodioxol-5-yl](II; R = CO2Et, R3 = H) as 1 of several diastereomers. The latter was N-alkylated by N-(2,4,6-trimethylphenyl)bromoacetamide (preparation given) to give, after saponification, II [R
= CO2H, R3 = N-(2,4,6-trimethylphenyl)carbamoylmethyl]. Data for biol.

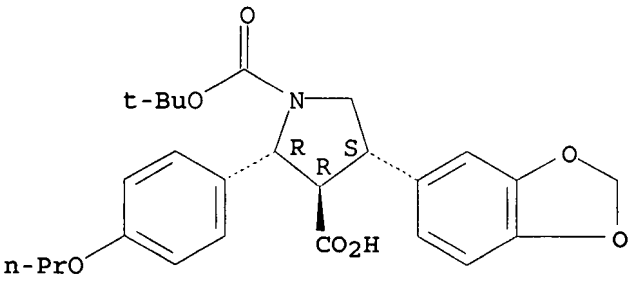
activity of I were given.

IT 195529-66-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-benzodioxolylpyrrolidine-3-carboxylates and analogs as endothelin receptor antagonists)

RN 195529-66-9 CAPLUS

CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-propoxyphenyl)-, 1-(1,1-dimethylethyl) ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L11 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1996:367754 CAPLUS

DN 125:86423

TI Regiochemical Control and Suppression of Double Bond Isomerization in the Heck Arylation of 1-(Methoxycarbonyl)-2,5-dihydropyrrole

AU Sonesson, Clas; Larhed, Mats; Nyqvist, Camilla; Hallberg, Anders

CS Department of Pharmacology, Medicinal Chemistry Unit, Goeteborg, S-413 90, Swed.

SO Journal of Organic Chemistry (1996), 61(14), 4756-4763
CODEN: JOCEAH; ISSN: 0022-3263

PB American Chemical Society

DT Journal

LA English

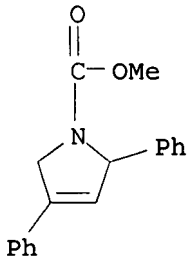
OS CASREACT 125:86423

AB Arylation of 1-(methoxycarbonyl)-2,5-dihydropyrrole under standard Heck reaction conditions produces a mixture of compds. The olefin undergoes two types of palladium-catalyzed reactions: (a) arylation to provide C-3 arylated derivs. and (b) competing double bond isomerization. Addition of silver carbonate and thallium acetate fully suppressed the isomerization, and good yields of C-3 substituted compds. were achieved after arylation with aryl halides. With regard to aryl triflates as arylating agents, addition of lithium chloride was necessary to promote the Heck reaction. This additive excluded the use of silver and thallium salts, but high regioselectivity and good yields could be obtained by employing tri-2-furylphosphine as ligand. Arylation was rendered both regioselective and enantioselective (58% ee) with 1-naphthyl triflate as substrate utilizing a (R)-BINAP/thallium acetate combination. The C-3 arylated enamides were converted further into the corresponding 3-arylpyrrolidines.

IT 178482-97-8P 178482-98-9P 178483-01-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

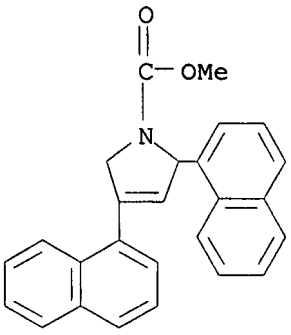
RN 178482-97-8 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2,5-dihydro-2,4-diphenyl-, methyl ester (9CI) (CA INDEX NAME)



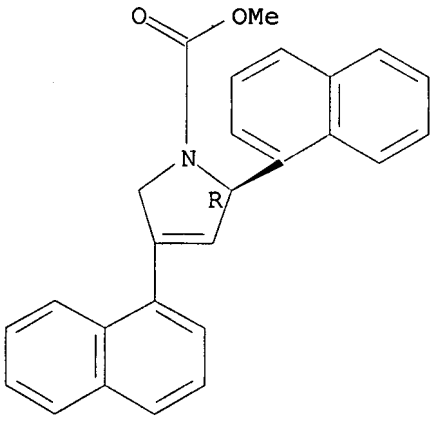
PRODUCED

RN 178482-98-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,5-dihydro-2,4-di-1-naphthalenyl-, methyl ester (9CI) (CA INDEX NAME)



RN 178483-01-7 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,5-dihydro-2,4-di-1-naphthalenyl-, methyl ester, (R)- (9CI) (CA INDEX NAME)

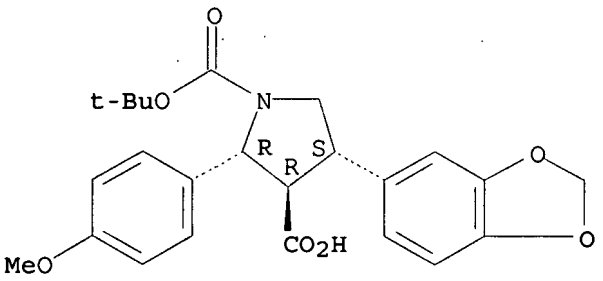
Absolute stereochemistry.



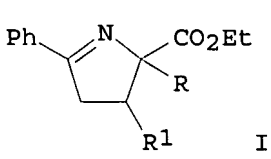
L11 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1996:95621 CAPLUS
DN 124:193286
TI 2,4-Diarylpyrrolidine-3-carboxylic Acids-Potent ETA Selective Endothelin Receptor Antagonists. 1. Discovery of A-127722
AU Winn, Martin; von Geldern, Thomas W.; Opgenorth, Terry J.; Jae, Hwan-Soo; Tasker, Andrew S.; Boyd, Steven A.; Kester, Jeffrey A.; Mantei, Robert A.; Bal, Radhika; et al.
CS Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, 60064, USA

SO Journal of Medicinal Chemistry (1996), 39(5), 1039-48
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB We have discovered a novel class of endothelin (ET) receptor antagonists through pharmacophore anal. of the existing non-peptide ET antagonists. On the basis of this anal., we determined that a pyrrolidine ring might replace the indan ring in SB 209670. The resultant compds. were readily prepared and amenable to extensive SAR studies. Thus a series of N-substituted trans,trans-2-(4-methoxyphenyl)-4-(1,3-benzodioxol-5-yl)pyrrolidine-3-carboxylic acids have been synthesized and evaluated for binding at ETA and ETB receptors. Compds. with N-acyl and simple N-alkyl substituents had weak activity. Compds. with N-alkyl substituents containing ethers, sulfoxides, or sulfones showed increased activity. Much improved activity resulted from compds. where the N-substituents were acetamides. A-127722, with the N,N-dibutylacetamide substituent is the best of the series. It has an IC50 = 0.36 nM for inhibition of ET-1 radioligand binding at the ETA receptor, with a 1000-fold selectivity for the ETA vs the ETB receptor. It is also a potent inhibitor (IC50 = 0.16 nM) of phosphoinositol hydrolysis stimulated by ET-1, and it antagonized the ET-1-induced contraction of the rabbit aorta with a pA2 = 9.20. The compound has 70% oral bioavailability in rats.
IT 173864-48-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; synthesis of diarylpyrrolidinecarboxylates as endothelin receptor antagonists)
RN 173864-48-7 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-, 1-(1,1-dimethylethyl) ester, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L11 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1991:449294 CAPLUS
DN 115:49294
TI Aryl and ethoxycarbonyl derivatives of pyrroles, 2H-pyrroles and 3,4-dihydropyrroles and their immunoactivity on human T lymphocytes
AU Birouk, M.; Harraga, S.; Panouse-Perrin, J.; Robert, J. F.; Damelincourt, M.; Theobald, F.; Mercier, R.; Panouse, J. J.
CS Equipe Chim. Ther., UFR Sci. Med. Pharm., Besancon, 25030, Fr.
SO European Journal of Medicinal Chemistry (1991), 26(1), 91-9
CODEN: EJMCA5; ISSN: 0223-5234
DT Journal
LA French
OS CASREACT 115:49294
GI



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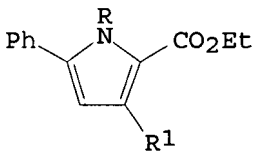
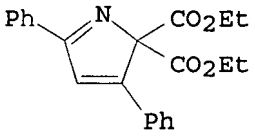


II



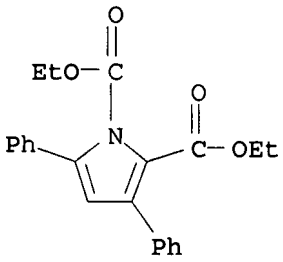
III

AB Title compds. I (R = CO2Et, R1 = H, Ph; R = H, R1 = Ph), II (R = H, CO2Et, R1 = Ph; R = H, R1 = CO2Et; R = CO2Et, R1 = H), and III were prepared I - III activate human T lymphocytes, II (R = H, R1 = Ph) having better activity than levamisole. A conformational approach based on magnetic anisotropy demonstrates the importance of the orthogonality of the substituent in the 3-position relative to the pyrrole ring for the immunostimulant activity.

IT 91307-93-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, decarboxylation, and immunostimulant activity of)

RN 91307-93-6 CAPLUS

CN 1H-Pyrrole-1,2-dicarboxylic acid, 3,5-diphenyl-, diethyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1990:157984 CAPLUS

DN 112:157984

TI Reactions of cobaltacyclopentadiene complexes with organic azides directed toward the synthesis of highly substituted pyrroles

AU Hong, Pangbu; Yamazaki, Hiroshi

CS Inst. Phys. Chem. Res., Wako, 351-01, Japan

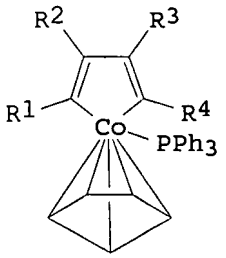
SO Journal of Organometallic Chemistry (1989), 373(1), 133-42
CODEN: JORCAI; ISSN: 0022-328X

DT Journal

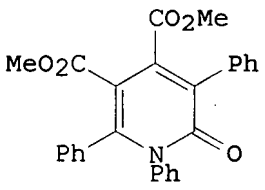
LA English

OS CASREACT 112:157984

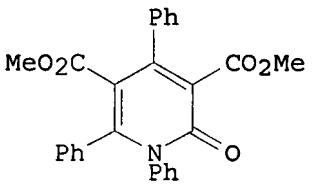
GI



I



VI



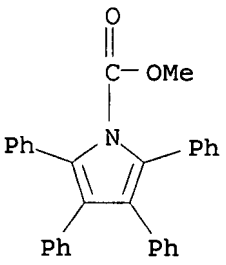
VII

AB The reactions of the cobaltacyclopentadiene complexes I [R1 = R2 = R3 = R4 = Ph (II); R1 = R4 = Ph, R2 = R3 = Me, CO2Me; R1 = R3 = Ph, R2 = R4 = CO2Me (III)] with organic azides were investigated. II reacts with Ph azide at 80° to give 1,2,3,4,5-pentaphenylpyrrole in 73% yield. Similarly, the reactions of II with benzoyl and tert-butoxycarbonyl azides give 1-benzoyl- and 1-(tert-butoxycarbonyl)-2,3,4,5-tetraphenylpyrroles in 41 and 64% yields, resp., but reaction with p-toluenesulfonyl azide gives 2,3,4,5-tetraphenylpyrrole and 3,4,5,6-tetraphenylpyridazine in 35 and 45% yields, resp., in place of the expected 1-(p-toluenesulfonyl)-2,3,4,5-tetraphenylpyrrole. The reaction of I (R1 = R4 = Ph, R2 = R3 = CO2CH3) (IV) with Ph azide at 130° gives 1,2,5-triphenyl-3,4-bis(methoxycarbonyl)pyrrole and 2,5-diphenyl-3,4-bis(methoxycarbonyl)pyrrole (V) in 22 and 15% yields, resp. The reaction of IV with benzenesulfonyl azide gives only V in 57% yield. In the reaction of III with benzenesulfonyl azide, V was unexpectedly obtained in 26% yield, together with 2,4-diphenyl-3,5-bis(methoxycarbonyl)pyrrole (30%), which suggests that a skeletal rearrangement of the metallacycle occurs during the reaction. The reaction of IV or III with benzoyl azide at 130° gives the 2(1H)-pyridinone derivs. VI (82%) and VII (53%), which are the products of the reaction of the corresponding cobaltacyclopentadiene with Ph isocyanate generated by the rearrangement of benzoyl nitrene, in place of the expected, corresponding pyrrole.

IT 126087-06-7P 126087-07-8P 126087-08-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

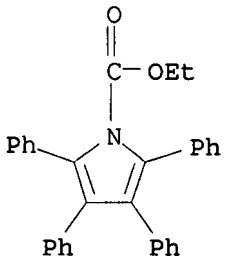
RN 126087-06-7 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2,3,4,5-tetraphenyl-, methyl ester (9CI) (CA INDEX NAME)

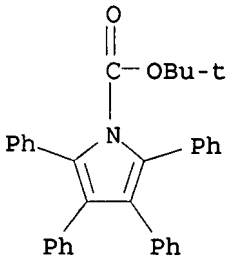


RN 126087-07-8 CAPLUS

CN 1H-Pyrrole-1-carboxylic acid, 2,3,4,5-tetraphenyl-, ethyl ester (9CI) (CA INDEX NAME)



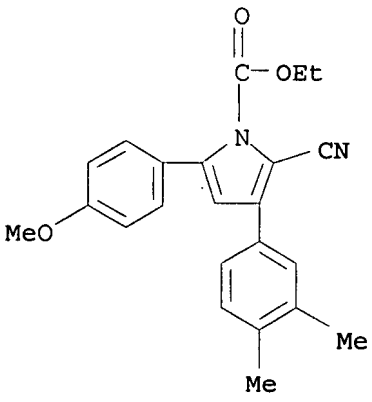
RN 126087-08-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2,3,4,5-tetraphenyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



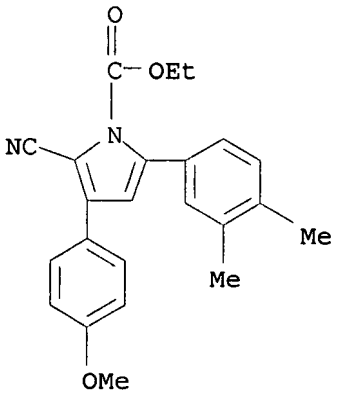
L11 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1988:94353 CAPLUS
DN 108:94353
TI The synthesis and chemistry of azolenines. Part 10. Reinvestigation of a reaction reported to yield ethyl 2-cyano-3-(3,4-dimethylphenyl)-5-(4-methoxyphenyl)-2H-pyrrole-2-carboxylate, and thermal rearrangements of this and a regioisomer
AU Ip, Shing Hong; Sammes, Michael P.
CS Dep. Chem., Univ. Hong Kong, Hong Kong, Hong Kong
SO Journal of Chemical Research, Synopses (1987), (10), 330-1
CODEN: JRPSDC; ISSN: 0308-2342
DT Journal
LA English
OS CASREACT 108:94353
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

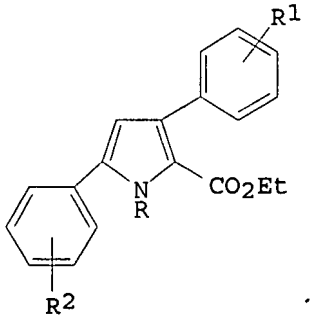
AB Reaction of chalcone I with NCCH2CO2Et and NH4OAc gave pyridines II and III, not pyrrolecarboxylate IV (Moussa, H. H.; Chabaka, L. M., 1983). Thermal rearrangement of IV gave pyrroles V (R = CO2Et, R1 = H; R = H, R1 = CO2Et).
IT 113019-48-0P 113019-50-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 113019-48-0 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2-cyano-3-(3,4-dimethylphenyl)-5-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 113019-50-4 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2-cyano-5-(3,4-dimethylphenyl)-3-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1988:74692 CAPLUS
DN 108:74692
TI The synthesis and chemistry of azolenines. Part 7. Carbon-13 NMR spectra of 3,5-diaryl-1H-pyrrole-2-carboxylic esters, and -1,2-dicarboxylic esters. Complete assignments and substituent chemical shift effects of 3- and 5-aryl ring substituents
AU Chung, Margaret W. L.; Sammes, Michael P.
CS Dep. Chem., Univ. Hong Kong, Hong Kong
SO Journal of Chemical Research, Synopses (1987), (9), 292-3
CODEN: JRPSDC; ISSN: 0308-2342
DT Journal
LA English
GI



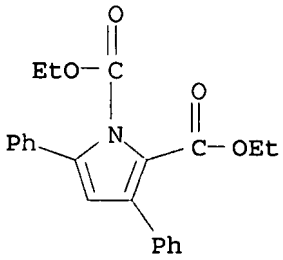
I

AB Diarylpyrrolecarboxylates I (R = H, CO2Et; R1, R2 = H, 3-NO2, 4-NO2, 4-Cl, 4-Me, 4-MeO) were prepared and their carbon-13 NMR chemical shifts were assigned. Substituent effects of ring substituents on chemical shifts were studied by using Hammett correlations.

IT 91307-93-6 100784-78-9 100784-79-0
100784-80-3 100784-81-4 100784-82-5
100784-83-6 100784-84-7 100784-85-8
100784-86-9 112798-46-6 112798-47-7
RL: PRP (Properties)
(carbon-13 NMR of)

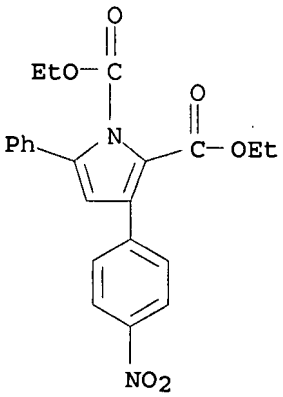
RN 91307-93-6 CAPLUS

CN 1H-Pyrrole-1,2-dicarboxylic acid, 3,5-diphenyl-, diethyl ester (9CI) (CA INDEX NAME)



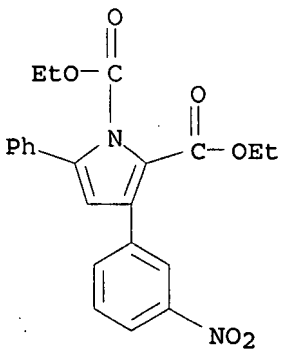
RN 100784-78-9 CAPLUS

CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-nitrophenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)

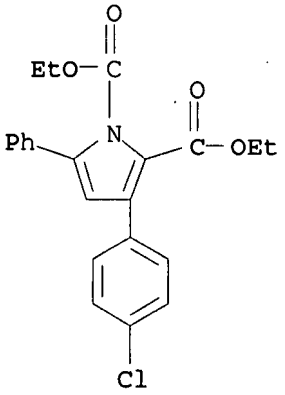


RN 100784-79-0 CAPLUS

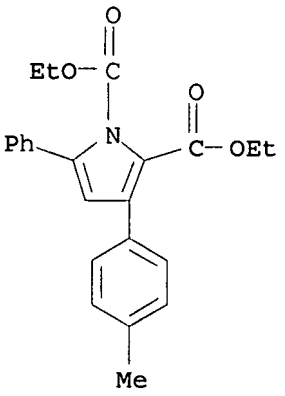
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(3-nitrophenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



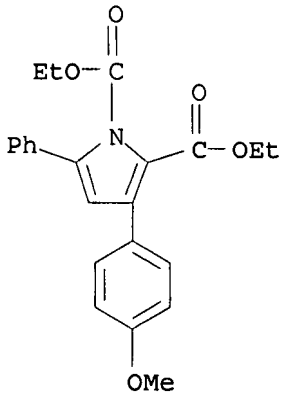
RN 100784-80-3 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-chlorophenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



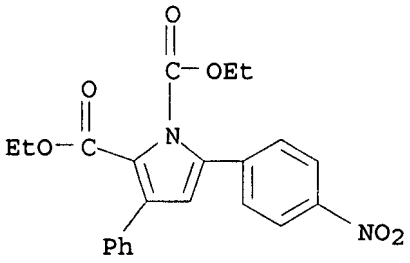
RN 100784-81-4 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-methylphenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



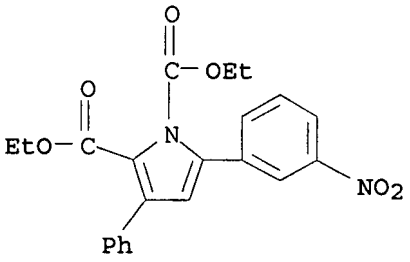
RN 100784-82-5 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-methoxyphenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



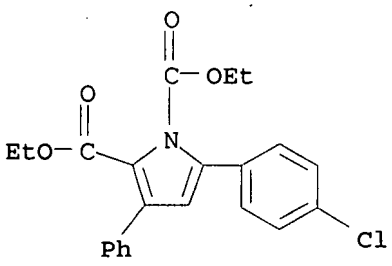
RN 100784-83-6 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(4-nitrophenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



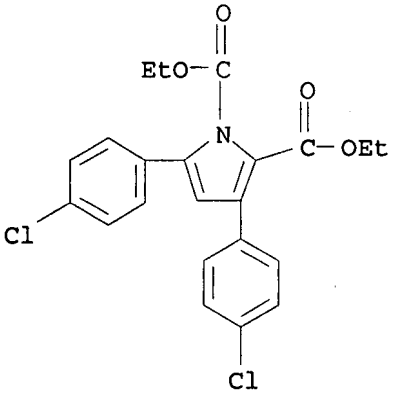
RN 100784-84-7 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(3-nitrophenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



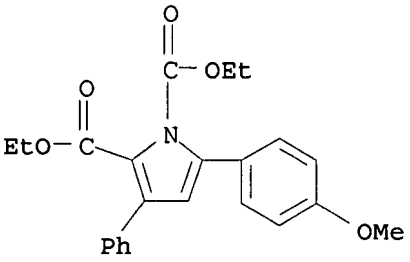
RN 100784-85-8 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(4-chlorophenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



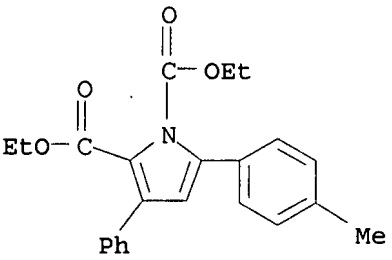
RN 100784-86-9 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3,5-bis(4-chlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 112798-46-6 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(4-methoxyphenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)

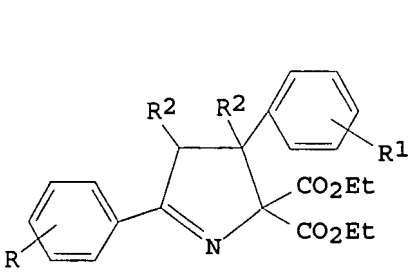


RN 112798-47-7 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(4-methylphenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)

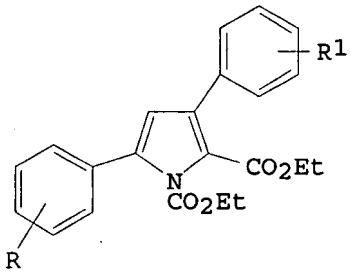


L101 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1986:109402 CAPLUS
DN 104:109402
TI The synthesis and chemistry of azolenines. Part 4. Preparation and rearrangement of some 3,5-diaryl-2H-pyrrole-2,2-dicarboxylic esters
AU Sammes, Michael P.; Chung, Margaret W. L.; Katritzky, Alan R.
CS Dep. Chem., Univ. Hong Kong, Hong Kong, Hong Kong
SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1985), (8), 1773-9
CODEN: JCPRB4; ISSN: 0300-922X

DT Journal
LA English
OS CASREACT 104:109402
GI



I



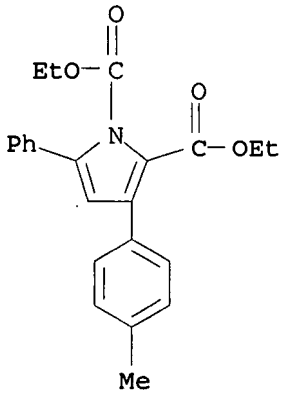
III

AB Oxidation of dihydropyrroles I (R = H, R1 = H, 4-NO2, 3-NO2, 4-Cl, 4-Me, 4-OMe; R = 4-NO2, 3-NO2, 4-Cl, R1 = H; R = R1 = 4-Cl; R2 = H) (II) with chloranil in refluxing xylene gave the rearranged products III (R, R1 as before) in 58-85% yield and not I (R, R1 as before, R22 = bond) (IV) as previously reported (Robert, J.F.; et al., 1978). IV were obtained from II in 58-82% yield on treatment with DDQ in C6H6 at room temperature IV rearranged to III in refluxing xylene by an acyl [1,5]-sigmatropic shift from C to N, a novel process in 2H-pyrroles. The rearrangement is concerted, with negligible charge separation in the transition state.

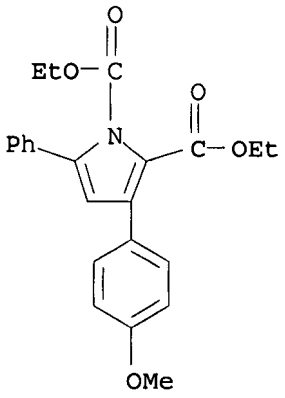
IT 100784-81-4P 100784-82-5P 100784-85-8P
100784-86-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and decarboxylation of)

RN 100784-81-4 CAPLUS

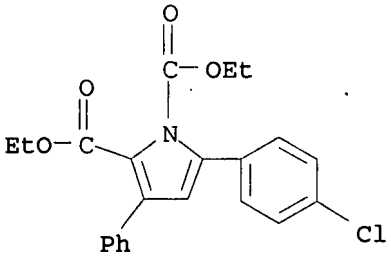
100784-81-4 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-methylphenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



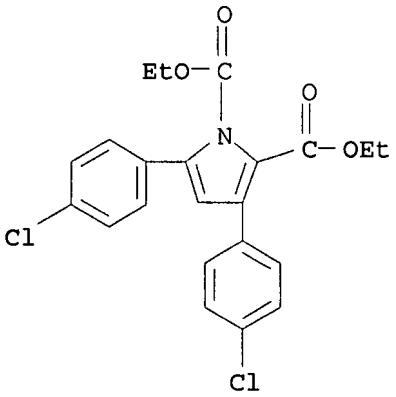
RN 100784-82-5 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-methoxyphenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



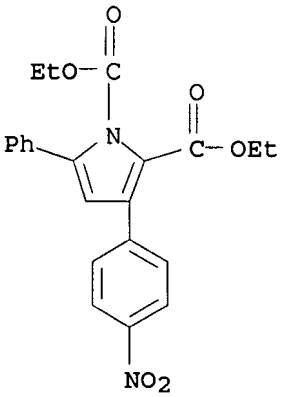
RN 100784-85-8 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(4-chlorophenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



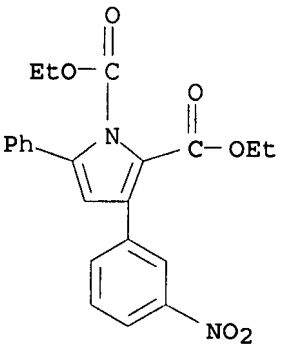
RN 100784-86-9 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3,5-bis(4-chlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



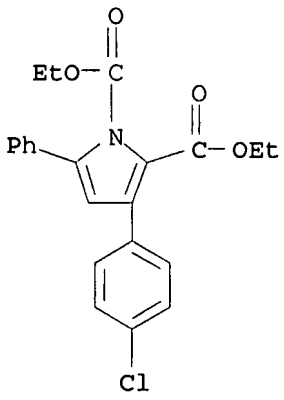
IT 100784-78-9P 100784-79-0P 100784-80-3P
100784-83-6P 100784-84-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 100784-78-9 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-nitrophenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



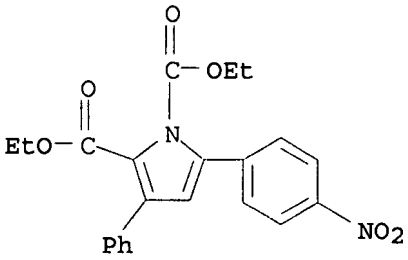
RN 100784-79-0 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(3-nitrophenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



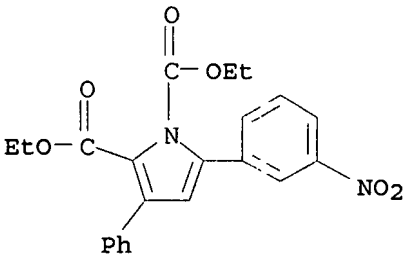
RN 100784-80-3 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(4-chlorophenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



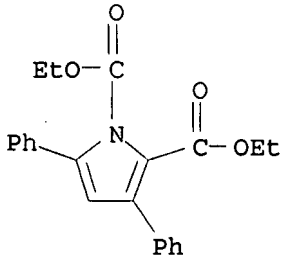
RN 100784-83-6 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(4-nitrophenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



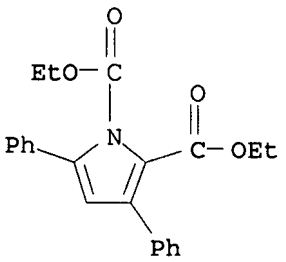
RN 100784-84-7 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 5-(3-nitrophenyl)-3-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



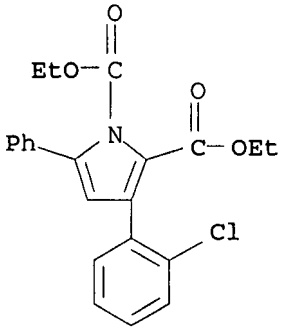
IT 91307-93-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, decarboxylation, and hydrolysis of)
RN 91307-93-6 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3,5-diphenyl-, diethyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1984:482038 CAPLUS
DN 101:82038
TI Compared structures of two pyrroles: diethyl 3,5-diphenylpyrrole-1,2-dicarboxylate, C22H21NO4 (1), and diethyl 3-(2-chlorophenyl)-5-phenylpyrrole-1,2-dicarboxylate, C22H20ClNO4 (2)
AU Laarif, Ahmed; Theobald, Francois; Birouk, Mohamed; Robert, Jean Francois
CS Lab. Chim. Gen., UER Sci. Exactes Nat., Besancon, 25030, Fr.
SO Acta Crystallographica, Section C: Crystal Structure Communications (1984), C40(7), 1278-81
CODEN: ACSCEE; ISSN: 0108-2701
DT Journal
LA French
AB Title compound 1 is orthorhombic, space group Pbca, with a 17.213(3), b 18.910(3), and c 11.968(3) Å; Z = 8 for dc = 1.239; Rw = 0.081 for 1762 reflections. Title compound 2 is also orthorhombic, space group Pbca, with a 16.955(3), b 18.487(4), and c 13.048(2) Å, Z = 8 for dc = 1.293. Rw = 0.067 For 3122 reflections. The modifications of the angles between the Ph groups and the pyrrole ring agree with the magnetic nonequivalence of the ethoxycarbonyl chains, which is more pronounced in 2. The 3 aromatic rings are planar. The carbonyl groups are planar: that attached to C(2) is coplanar with the pyrrole ring plane, but that attached to N is inclined to the ring plane by 72.4(7)° for 1 and 67.0(4)° for 2. Atomic coordinates are given.
IT 91307-93-6 91307-94-7
RL: PRP (Properties)
(structure of)
RN 91307-93-6 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3,5-diphenyl-, diethyl ester (9CI) (CA INDEX NAME)



RN 91307-94-7 CAPLUS
CN 1H-Pyrrole-1,2-dicarboxylic acid, 3-(2-chlorophenyl)-5-phenyl-, diethyl ester (9CI) (CA INDEX NAME)



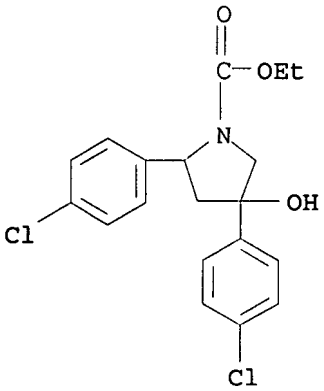
L11 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1964:23242 CAPLUS
DN 60:23242
OREF 60:4086h,4087a-g,4088a-g
TI Pyrrolidines. IX. 3-Aryl-3-pyrrolidinols
AU Gould, William A.; Lish, Paul M.; Wu, Yao-Hua; Roth, Herbert R.; Lobeck, Walter G., Jr.; Berdahl, James M.; Feldkamp, Rolland F.
CS Mead Johnson Res. Center, Evansville, IN
SO Journal of Medicinal Chemistry (1964), 7(1), 60-7
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 57, 12412a. 3-Aryl-3-hydroxy-1-pyrrolidinecarboxylic acid esters were hydrolyzed and decarboxylated in the presence of a strong base to produce the tabulated 3-aryl-3-pyrrolidinols. These substances exhibited central nervous system stimulant activity and smooth muscle depressant action variously selective for smooth muscle of the bronchioles, uterus, gut, and the coronary and peripheral vascular system. R1, R2, R3, Salt, M.p., % Yield; H, H, Ph, HCl, 147-7°, 46; H, H, Cyclohexyl, HCl, 179-81°, 46; H, H, 2-Thienyl, HCl, 163-5°, 37; H, H, 4-ClC6H4, HCl, 170.5-72°, 89; H, H, 3-ClC6H4, HCl, 173-5°, 86; H, H, 2-ClC6H4, HCl, 238.5-39° (decomposition), 82; H, H, 4-BrC6H4, HCl, 187.5-8.5°, 90; H, H, 4-FC6H4, HCl, 182-3° (decomposition), 80; H, H, 3-F3CC6H4, HCl, 162.5-4°, 88; H, H, 3,4-Cl2C6H3, HCl, 188-9.5°, 95; H, H, 4-MeC6H4, HCl, 153-4°, 90; H, H, 2-MeC6H4, HCl, 199-9.5 (decomposition), 82; H, H, 2,5-Me2C6H3, HCl, 218-19° (decomposition), 83; H, H, 2-MeOC6H4, HCl, 138.5-9.5° (decomposition), 49; H, H, 4-EtOC6H4, HCl, 125.5-6.5° (decomposition), 74; H, H, 4-PhCH2OC6H4, benzoate, 187-9°, 83; H, H, 3-PhCH2OC6H4, benzoate, 133-5°, 76; H, H, 4-HOC6H4, benzoate, 164-5° (decomposition), 60; H, H, 3-HOC6H4, benzoate, 209.5-11.5° (decomposition), 89; H, H, 4-ClC6H4CH2, HCl, 187-8°, 74; Me, H, Ph, HCl, 196-8°, 52; Me, H, PhCH2, HCl, 188-90.5°, 62; Me, H, 4-ClC6H4, HCl, 205-7°, 82; Me, H, 3-ClC6H4, HCl, 180-2°, 89; Me, H, 2-ClC6H4, HCl, 251.5-3.5° (decomposition), 87; Me, H, 3-F3CC6H4, HCl, 199.5-201.5°, 87; Me, H, 3,4-Cl2C6H3, HCl, 268-9° (decomposition), 91; Me, H, 4-MeC6H4, HCl, 205.5-207°, 66; Me, H, 2-MeC6H4, HCl.0.5H2O, 218-19.5° (decomposition), 70; Me, H, 2,5-Me2C6H3, HCl, 190.5-92°, 39; Me, H, 4-MeOC6H4, HCl, 190-90.5° (decomposition), 82; Me, H, 2-MeOC6H4, HCl, 221-3° (decomposition), 43; Me, H, 4-EtOC6H4, HCl, 176.5-8.5° (decomposition), 61; Me, H, 4-PhOC6H4, HCl, 239-9.5° (decomposition), 40; Me, H, 4-PhCH2OC6H4, HCl, 214-15° (decomposition), 90; Me, H, 4-PhCH2OC6H4, benzoate, 164-6°, 79; Me, H, 3-PhCH2OC6H4, HCl, 138.5-40°, 94; Me, H, 4-HOC6H4, benzoate, 202.5-4.5° (decomposition), 62; Me, H, 3-HOC6H4, HCl, 232-3° (decomposition), 93; Me, H, 4-(4-ClC6H4CH2O)C6H4, HCl, 211-12° (decomposition), 72; Me, H, 3,4-Isopropylidenedioxyphenyl, , 126.5-8.5°, 37; Me, H, 3,4-Isopropylidenedioxyphenyl, benzoate,

193-6° (decomposition), 90; Me, H, 4-MeSC6H4, , 157-9°, 57; Me, H, 4-MeSC6H4, HCl, 204.5-6.5° (decomposition), 75; Me, H, 4-PhC6H4, HCl, 250-1° (decomposition), 55; H, Me, Ph, HCl, 152.5-54°, 74; H, Me, 4-ClC6H4, HCl, 179-81°, 59; H, Me, 3-ClC6H4, HCl, 158-60°, 79; H, Me, 2-ClC6H4, HCl, 203-5° (decomposition), 79; H, Me, 4-BrC6H4, , 141-3°, 73; H, Me, 4-BrC6H4, HCl, 204.5-5.5° (decomposition), 95; H, Me, 4-FC6H4, HCl, 145-7°, 60; H, Me, 3,4-Cl2C6H8, HCl, 191-2°, 90; H, Me, 4-PhCH2OC6H4, , 160-2°, 65; H, Me, 4-PhCH2OC6H4, benzoate, 167-9°, 93; H, Me, 4-PhCH2OC6H4, HCl, 182-2.5° (decomposition), 71; H, Me, 4-HOC6H4, HCl, 207-9° (decomposition), 40; Et, H, Ph, HCl, 248.5-49° (decomposition), 60; Et, H, 4-ClC6H4, HCl, 235-6.5° (decomposition), 80; Et, H, 4-PhCH2OC6H4, benzoate, 163-5°, 73; Et, H, 4-HOC6H4, benzoate, 174.5-6.5° (decomposition), 95; H, Et, Ph, HCl, 187-8°, 80; H, Et, 4-ClC6H4, HCl, 173-5°, 86; H, iso-Pr, Ph, HCl, 226.5-7.5° (decomposition), 48; H, iso-Pr, 4-ClC6H4, HCl, 206.5-7.5 (decomposition), 35; Me, Me, Ph, HCl, 232.5-3.5° (decomposition), 68; Me, Me, 4-ClC6H4, HCl, 251-2° (decomposition), 84; Me, Me, 4-ClC6H4, HCl, 222.5-4.5° (decomposition), 46; Me, Me, 4-PhCH2OC6H4, HCl, 248.5-49° (decomposition), 61; Me, Me, 4-HOC6H4, HCl, 221.5-23° (decomposition), 69; Et, Me, Ph, HCl, 269.5-70° (decomposition), 65; Et, Me, 4-ClC6H4, HCl, 276-6.5° (decomposition), 42; H, 3-Cyclohexenyl, Ph, HCl, 232.5-3.5° (decomposition), 26; H, 3-Cyclohexenyl, 4-ClC6H4, HCl, 252.5-53° (decomposition), 37; H, Cyclohexyl, Ph, HCl, 226.5-27° (decomposition), 47; H, Cyclohexyl, 4-ClC6H4, HCl, 252.5-53° (decomposition), 95; H, Ph, Ph, HCl, 207-8° (decomposition), 47; H, Ph, 4-ClC6H4, HCl, 204-5° (decomposition), 85; H, Ph, 3,4-Cl2C6H3, , 157-9°, 74; H, Ph, 3,4-Cl2C6H3, HCl, 201-3° (decomposition), 95; H, Ph, 3-F3CC6H4, , 147-9°, 78; H, Ph, 3-F3CC6H4, HCl, 203-4.5° (decomposition), 77; Me, Ph, Ph, HCl, 275-6° (decomposition), 62; H, 4-ClC6H4, Ph, , 160-2°, 88; H, 4-ClC6H4, Ph, HCl, 207-7.5° (decomposition), 90; H, 4-ClC6H4, 4-ClC6H4, HCl, 204-4.5° (decomposition), 67; H, 4-MeOC6H4, Ph, HCl, 164-6° (decomposition), 95; H, 3,4-CH2O2C6H3, Ph, , 150-2°, 95; H, 3,4-CH2O2C6H3, Ph, HCl, 215-16° (decomposition), 92; H, 3,4-CH2O2C6H3, 4-ClC6H4, , 161-2°, 75; H, 3,4-CH2O2C6H3, 4-ClC6H4, HCl, 215-16.5° (decomposition), 99;

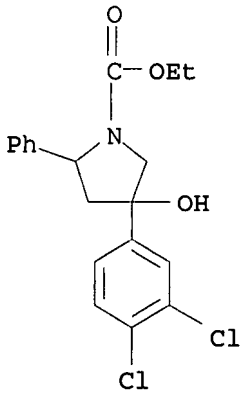
IT 94303-88-5P, 1-Pyrrolidinecarboxylic acid, 2,4-bis(p-chlorophenyl)-4-hydroxy-, ethyl ester 94303-89-6P, 1-Pyrrolidinecarboxylic acid, 4-(3,4-dichlorophenyl)-4-hydroxy-2-phenyl-, ethyl ester 94577-12-5P, 1-Pyrrolidinecarboxylic acid, 3-hydroxy-2-methyl-3,5-diphenyl-, ethyl ester 95696-33-6P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-[3,4-(methylenedioxy)phenyl]-4-phenyl-, ethyl ester
RL: PREP (Preparation)
(preparation of)

RN 94303-88-5 CAPLUS

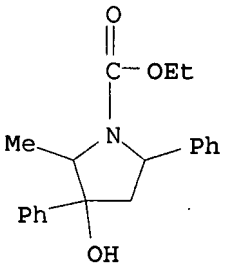
CN 1-Pyrrolidinecarboxylic acid, 2,4-bis(p-chlorophenyl)-4-hydroxy-, ethyl ester (7CI) (CA INDEX NAME)



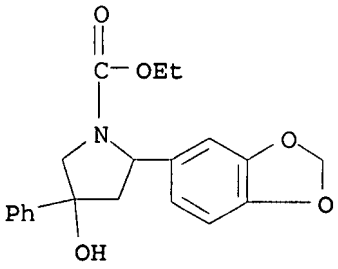
RN 94303-89-6 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-(3,4-dichlorophenyl)-4-hydroxy-2-phenyl-, ethyl ester (7CI) (CA INDEX NAME)



RN 94577-12-5 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-2-methyl-3,5-diphenyl-, ethyl ester (7CI) (CA INDEX NAME)



RN 95696-33-6 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-[3,4-(methylenedioxy)phenyl]-4-phenyl-, ethyl ester (7CI) (CA INDEX NAME)



L11 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1963:448277 CAPLUS
DN 59:48277
OREF 59:8709b-g
TI 1-Acyl and 1-carbalkoxy-3-pyrrolidinols
IN Wu, Yao-Hua; Feldkamp, Rolland F.; Lobeck, Walter G., Jr.
PA Mead Johnson & Co.
SO 8 pp.

DT Patent
LA Unavailable
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3083208		19630326	US 1961-109269	19610511
PRAI US		19610511		

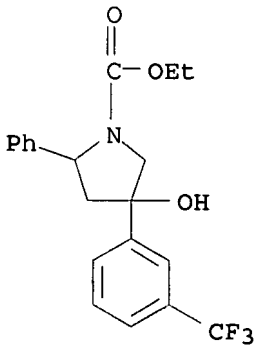
AB The title compds. are prepared by treating a suitable 1-acyl or 1-carbalkoxy-3-pyrrolidinone with an appropriate Grignard reagent and hydrolyzing the resultant Grignard complex. The compds. were found to have pronounced hypnotic activity. Thus, an ethereal solution of PhMgBr from 69 g. PhBr, 11.7 g. Mg, and 125 ml. anhydrous Et2O was added dropwise in 1 hr. to 62.9 g. 1-carbethoxy-3-pyrrolidinone in 100 ml. anhydrous Et2O, the mixture stirred and refluxed 3 hrs. and poured into 600 g. ice containing 30 g. NH4Cl, the ethereal layer dried, filtered, and concentrated, the residue distilled in vacuo, and the fraction, b0.15 132-80°, treated with Me2CO to give 30 g. 1-carbethoxy-3-phenyl-3-pyrrolidinol, m. 87-9°. Similarly prepared were: 1-carbethoxy-3-p-chlorophenyl-3-pyrrolidinol, m. 95-7°; 1-carbethoxy-3-p-anisyl-3-pyrrolidinol, m. 77-9°; 1-carbethoxy-3-p-tolyl-3-pyrrolidinol, m. 74-6°; 1-carbethoxy-3-(2-thienyl)-3-pyrrolidinol, m. 79-81°; 1-carbethoxy-3-p-benzyloxyphenyl-3-pyrrolidinol, m. 126-7°; 1-carbethoxy-2-methyl-3-benzyl-3-pyrrolidinol, b0.15 145-7°; 1-carbethoxy-3,5-diphenyl-3-pyrrolidinol, m. 151-3°; 1-carbethoxy-3-phenyl-5-methyl-3-pyrrolidinol, m. 126-7°. N-Carbethoxy-DL-α-alanine Et ester (I), b27 140.5-142.0°, n25D 1.4332, was obtained by treating DL-α-alanine Et ester with ClCO2Et. I was refluxed with NaH and CH2:CHCO2Et in C6H6 to give 1,4-dicarbethoxy-2-methyl-3-pyrrolidinone (II), b0.2 106-25°, n25D 1.4652. II was converted to 1-carbethoxy-2-methyl-3-pyrrolidinone (III), b14 126-30°, n25D 1.4598. III was made to react with PhMgBr to yield 1-carbethoxy-2-methyl-3-phenyl-3-pyrrolidinol, m. 95-7°. Similarly prepared were: 1-carbethoxy-2-methyl-3-o-tolyl-3-pyrrolidinol, b0.5 152-5°; 1-carbethoxy-2-methyl-3-p-anisyl-3-pyrrolidinol, m. 103-5°; 1-carbethoxy-2-methyl-3-m-chlorophenyl-3-pyrrolidinol, m. 93-5°. 1-Carbomethoxy-3-phenyl-3-pyrrolidinol (IV), m. 94-6°, was similarly prepared by the sequence of steps N-carbomethoxyglycine Et ester, b17 137-9°, n25D 1.4370 → 1-carbomethoxy-4-carbethoxy-3-pyrrolidinone, b0.15 105-10° → 1-carbomethoxy-3-pyrrolidinone, m. 59-63° → IV. Similarly prepared were: 1-carbisobutoxy-3-phenyl-3-pyrrolidinol (V), b0.4 170-2°, by the sequence of steps: N-carbisobutoxyglycine Et ester, b17 150-4°, n25D 1.4367 → 1-carbisobutoxy-4-carbethoxy-3-pyrrolidinone, b0.5 135-243°, n25D 1.4676 → 1-carbisobutoxy-3-pyrrolidinone, b15 154-8°, n25D 1.4620, m. 25-35° → V; 1-carbisobutoxy-3-p-chlorophenyl-3-pyrrolidinol, b0.2 195-200°; 1-carbethoxy-2,5-dimethyl-3-phenyl-3-pyrrolidinol (VI), b0.2 130-5°, by the sequence of steps 1,4-dicarbethoxy-2,5-dimethyl-3-pyrrolidinone, b0.2 86-7°, n25D 1.4672 → 1-carbethoxy-2,5-dimethyl-3-pyrrolidinone, b22 130-2°, n25D 1.4550 → VI; 1-acetyl-3-phenyl-3-pyrrolidinol(VII), b0.1 172-4°, by the sequence of steps 1-acetyl-4-carbethoxy-3-pyrrolidinone, b0.5 154-64°, m. 55-7° → 1-acetyl-3-pyrrolidinone, b0.55 120-3°, n25D 1.4978 → VII; 1-acetyl-2-methyl-3-phenyl-3-pyrrolidinol (VIII), m. 143-5°, by the sequence of steps 1-acetyl-2-methyl-4-carbethoxy-3-pyrrolidinone, b0.15 105-7°, n25D 1.4830 → 1-acetyl-2-methyl-3-pyrrolidinone, b0.15 83-7°, n25D 1.4850 → VIII; 1-carbethoxy-2-ethyl-3-phenyl-5-methyl-3-pyrrolidinol (IX), m. 111-16°, by the sequence of steps Et N-carbethoxy-DL-α-aminobutyrate, b22 144-6°, n25D 1.4365 → 1,4-dicarbethoxy-2-ethyl-5-methyl-3-pyrrolidinone, b0.25 101-5°, n25D 1.4684 → 1-carbethoxy-2-ethyl-5-methyl-3-pyrrolidinone, b20 140-1°, n25D 1.4557 → IX. Addnl. 62

compds. were prepared and are listed, which are all 1-carbethoxy derivs.

IT 1765-54-4P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-phenyl-4-(α,α,α-trifluoro-m-tolyl)-, ethyl ester
94303-88-5P, 1-Pyrrolidinecarboxylic acid, 2,4-bis(p-chlorophenyl)-4-hydroxy-, ethyl ester 94303-89-6P, 1-Pyrrolidinecarboxylic acid, 4-(3,4-dichlorophenyl)-4-hydroxy-2-phenyl-, ethyl ester 94311-45-2P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2,4-diphenyl-, ethyl ester 94384-09-5P, 1-Pyrrolidinecarboxylic acid, 2-(p-chlorophenyl)-4-hydroxy-4-phenyl-, ethyl ester 94384-10-8P, 1-Pyrrolidinecarboxylic acid, 4-(p-chlorophenyl)-4-hydroxy-2-phenyl-, ethyl ester 94549-08-3P, 1-Pyrrolidinecarboxylic acid, 4-(p-chlorophenyl)-4-hydroxy-2-[3,4-(methylenedioxy)phenyl]-, ethyl ester 94577-12-5P, 1-Pyrrolidinecarboxylic acid, 3-hydroxy-2-methyl-3,5-diphenyl-, ethyl ester 94577-37-4P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-(p-methoxyphenyl)-4-phenyl-, ethyl ester 95696-33-6P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-[3,4-(methylenedioxy)phenyl]-4-phenyl-, ethyl ester 96675-07-9P, 1-Pyrrolidinecarboxylic acid, 4-[p-(benzyloxy)phenyl]-2-(p-chlorophenyl)-4-hydroxy-, ethyl ester
RL: PREP (Preparation)
(preparation of)

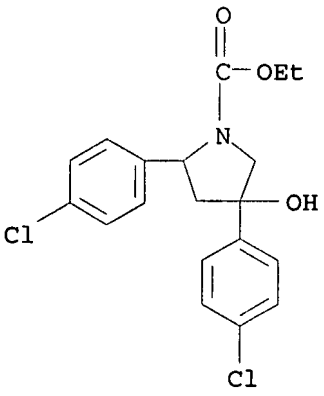
RN 1765-54-4 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-phenyl-4-(α,α,α-trifluoro-m-tolyl)-, ethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 94303-88-5 CAPLUS

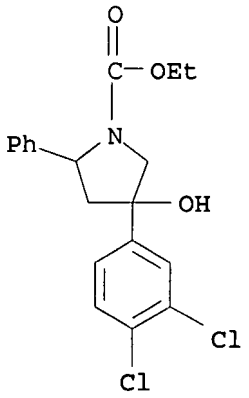
CN 1-Pyrrolidinecarboxylic acid, 2,4-bis(p-chlorophenyl)-4-hydroxy-, ethyl ester (7CI) (CA INDEX NAME)



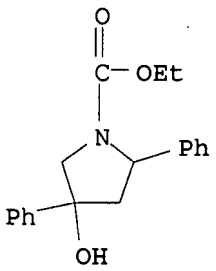
RN 94303-89-6 CAPLUS

CN 1-Pyrrolidinecarboxylic acid, 4-(3,4-dichlorophenyl)-4-hydroxy-2-phenyl-,

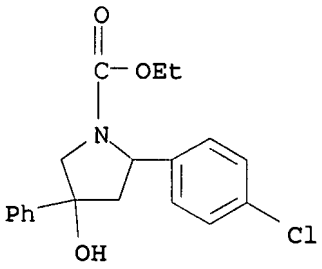
ethyl ester (7CI) (CA INDEX NAME)



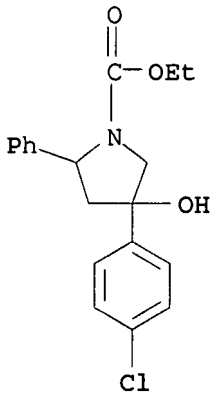
RN 94311-45-2 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2,4-diphenyl-, ethyl ester (7CI)
(CA INDEX NAME)



RN 94384-09-5 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-(p-chlorophenyl)-4-hydroxy-4-phenyl-,
ethyl ester (7CI) (CA INDEX NAME)



RN 94384-10-8 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-(p-chlorophenyl)-4-hydroxy-2-phenyl-,
ethyl ester (7CI) (CA INDEX NAME)



RN 94549-08-3 CAPLUS
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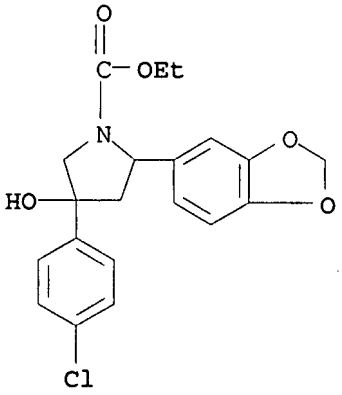
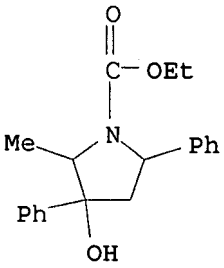
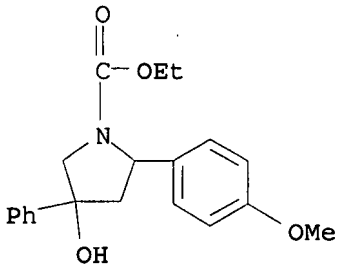


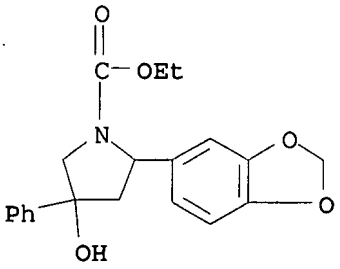
RN 94577-12-5 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-2-methyl-3,5-diphenyl-, ethyl ester (7CI) (CA INDEX NAME)



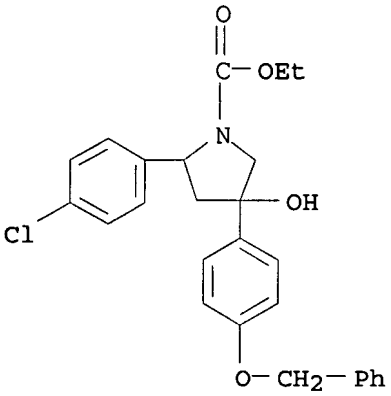
RN 94577-37-4 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-(p-methoxyphenyl)-4-phenyl-, ethyl ester (7CI) (CA INDEX NAME)



RN 95696-33-6 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-[3,4-(methylenedioxy)phenyl]-4-phenyl-, ethyl ester (7CI) (CA INDEX NAME)



RN 96675-07-9 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[p-(benzyloxy)phenyl]-2-(p-chlorophenyl)-4-hydroxy-, ethyl ester (7CI) (CA INDEX NAME)



L11 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1962:483165 CAPLUS
DN 57:83165
OREF 57:16566a-i,16567a-b
TI 1-Acyl and 1-carbalkoxy-3-pyrrolidinols
PA Mead Johnson & Co.
SO 8 pp.
DT Patent
LA Unavailable
FAN.CNT 1

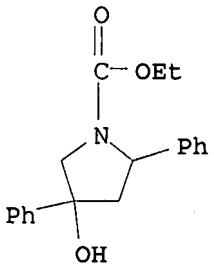
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 873303		19610719	GB 1959-36542	19591028

DE 1125429 DE
PRAI US 19590212
GI For diagram(s), see printed CA Issue.
AB The prepns. of I are described. A mixture of 100 g. DL-α-alanine, 115.5 g. anhydrous HCl, and 450 ml. absolute EtOH was refluxed 5 hrs., and evaporated nearly to dryness under reduced pressure. The residue was treated with three 100 ml. portions of 95% EtOH and the EtOH removed. H2O (200 ml.) was added, the aqueous solution cooled in all ice bath, neutralized with 116 ml. 10N NaOH, ClCO2Et added dropwise with stirring in 2 hrs., the mixture stirred for a further hr., and then stirred 10 min. with 320 ml. 20% Na2CO3 solution and extracted with Et2O. The combined Et2O extract, after drying with anhydrous MgSO4 and filtering, was fractionated in vacuo to give 148.4 g. N-carbethoxyalanine Et ester (II), b27 140.5-2.0°, n25D 1.4332. Similarly prepared was Et N-carbethoxy-DL-α-aminobutyrate, b22 144-6°, n25D 1.4365. A solution of 69.8 g. glycine Et ester-HCl in 70 ml. H2O was neutralized with 50 ml. 40% NaOH and, while the temperature was kept under 10°, 42.3 g. ClCO2Me was added dropwise with stirring in 2 hrs., the mixture stirred for a further 30 min., 50 ml. 40% NaOH added and the mixture extracted with Et2O. The Et2O extract was dried over anhydrous MgSO4, filtered, concentrated, and fractionally distilled to give 27 g. N-carbomethoxyglycine Et ester, b17137-9°, n25D 1.4370. Similarly prepared was N-carbisobutoxyglycine Et ester, b17 150-4° n25D 1.4367. II (94.6 g.) was added dropwise to a suspension of NaH (52.8% pure, 22.3 g.) in 375 ml. dry C6H6, at a suitable rate to maintain gentle reflux. The mixture was refluxed a further 30 min., cooled and 50.1 g. Et acrylate added dropwise with stirring. The reaction mixture was stirred a further 30 min. and then refluxed 2 hrs. An equivalent amount of 3N HCl (167 ml.) was added and the mixture thoroughly shaken before the C6H6 layer was decanted and the aqueous layer extracted with CHCl3. The combined C6H6 and CHCl3 solution was dried over anhydrous MgSO4, filtered, and concentrated Distillation of the residue gave 83 g. 1,4-dicarbethoxy-2-methyl-3-pyrrolidinone (III), b0.2 106-25°, n25D 1.4652. The following substituted 3-pyrrolidinones were similarly prepared: 1-carbomethoxy-4-carbethoxy-, b0.15 105-10°; 1-carbisobutoxy-4-carbethoxy-, b0.3 135-43°, n25D 1.4676; 1,4-dicarbethoxy-2,5-dimethyl-, b0.2 86-7°, n25D 1.4672; 1-acetyl-4-carbethoxy-, m. 55-7°; 1-acetyl-4-carbethoxy-2-methyl-, b0.15 105-7°, n25D 1.4830; 1,4-dicarbethoxy-2-ethyl-5-methyl-, b0.25 101-5°, n25D 1.4684. A mixture of 83 g. III and 300 ml. H2O containing 3 ml. concentrated HCl was refluxed 15 hrs., the solution saturated with NaCl and extracted with 250 ml. CHCl3. The CHCl3 extract was dried over anhydrous MgSO4, filtered, concentrated and fractionated to give 43.5 g. 1-carbethoxy-2-methyl-3-pyrrolidone, (IV), b14 126-30°, n25D 1.4598. The following substituted 3-pyrrolidinones were similarly prepared: 1-carbomethoxy-, m. 59-63°; 1-carbisobutoxy-, b15 154-8°, n25D 1.4620; 1-carbethoxy-2,5-dimethyl-, b22 130-2°, n25D 1.4550; 1-acetyl-, b0.55 120-3°, n25D 1.4978; 1-acetyl-2-methyl-, b0.15 83-7°, n25D 1.4850; 1-carbethoxy-2-ethyl-5-methyl-, b20 140-1°, n25D 1.4557. A solution of PhMgBr, prepared from 69 g. PhBr, 11.7 g. Mg and 125 ml. Et2O was added dropwise in 1 hr. with stirring to 62.9 g. 1-carbethoxy-3-pyrrolidinone (prepared by method of Kuhn and Osswald, CA 51, 5752a, in 100 ml. anhydrous Et2O. The mixture was stirred and refluxed 3 hrs., and then added to 600 g. ice containing 30 g. NH4Cl. The Et2O layer was dried over anhydrous MgSO4, filtered and concentrated Fractional distillation in vacuo gave 37

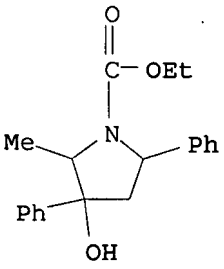
g. viscous oil, b0.15 132-80°, which yielded 30 g. 1-carbethoxy-3-phenyl-3-pyrrolidinol, m. 87-9°. The following 1-carbethoxy-3-(R-substituted)-3-pyrrolidinols were similarly prepared (R, and b.p./mm. or m.p. given): Et, 116-18°/0.08; p-ClC6H4, 95-7°; p-anisyl, 77-9°; p-tolyl, 74-6°. Similarly prepared were the following 1-carbethoxy-2-methyl-3-(R-substituted)-3-pyrrolidinols (R, b.p./mm. or m.p. given): Ph, 95-7° (iso-PrOH); o-tolyl, 152-5°/0.5, p-anisyl, 99-101°; m-ClC6H4, 93-5°; benzyl, 148-53°/0.15. The following substituted 3-pyrrolidinols: 1-carbomethoxy-3-phenyl-, 94-6°; 1-carbisobutoxy-3-phenyl-, 170-2°/0.4; 1-carbisobutoxy-3-(p-chlorophenyl)-, 195-200°/0.2; 1-carbethoxy-2,5-dimethyl-3-phenyl-, 130-5°/0.2; 1-acetyl-3-phenyl-, 172-4°/0.1; 1-acetyl-2-methyl-3-phenyl-, 143-5°; 1-carbethoxy-3,5-diphenyl-, 151-3°; 1-carbethoxy-5-methyl-3-phenyl-, 126-7°; 1-carbethoxy-2-ethyl-5-methyl-3-phenyl-, m. 111-16°.

IT 94311-45-2P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2,4-diphenyl-, ethyl ester 94577-12-5P, 1-Pyrrolidinecarboxylic acid, 3-hydroxy-2-methyl-3,5-diphenyl-, ethyl ester
RL: PREP (Preparation)
(preparation of)

RN 94311-45-2 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2,4-diphenyl-, ethyl ester (7CI) (CA INDEX NAME)

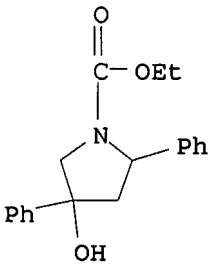


RN 94577-12-5 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 3-hydroxy-2-methyl-3,5-diphenyl-, ethyl ester (7CI) (CA INDEX NAME)



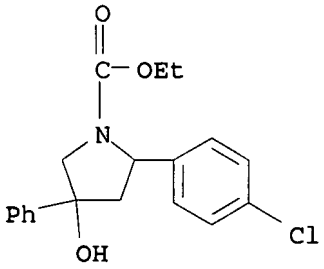
L[illegible] ANSWER 42 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1962:462595 CAPLUS
DN 57:62595
OREF 57:12412a-e
TI Pyrrolidines. VII. 3-Hydroxy-1-pyrrolidine carboxylic acid esters
AU Wu, Yao-Hua; Gould, William A.; Lobeck, Walter G., Jr.; Roth, Herbert R.; Feldkamp, R. F.
CS Mead Johnson Res. Center, Evansville, IN

SO Journal of Medicinal & Pharmaceutical Chemistry (1962), 5, 752-62
CODEN: JMPCAS; ISSN: 0095-9065
DT Journal
LA Unavailable
OS CASREACT 57:62595
AB cf. CA 57, 7263g. The title compds. were prepared by a 4-step reaction from Nalkoxycarbonylamino acid esters and tested as hypnotic agents. 4-Chlorobenzaldehyde (100 g.), 150 g. malonic acid, 5 ml. piperidine, and 300 ml. pyridine were heated on a steam bath 3 hrs., refluxed 31) min., cooled, poured into 4 l. ice H2O containing 380 ml. concentrated HCl, the precipitate filtered off, washed with H2O, stirred with 700 ml. 10% anhydrous EtOHHCl, refluxed 20 hrs., the solvent removed, the residue dissolved in Et2O, the solution washed with 10% NaOH, dried, filtered, concentrated, and distilled in vacuo to give 128.3 g. ethyl 4-chlorocinnamate, b22 178-9°. Ethyl 2-pentenoate, b. 156-8°, was prepared similarly. Benzyl chloride (36.5 g., 50 g. 3-bromophenol, 40 g. K2CO3, and 25 ml. Me2CO were refluxed 5 hrs., cooled, treated with 500 ml. H2O, extracted with Et2O, the exts. washed with 100 ml. 10% NaOH and H2O, dried, the solvent removed, and the residue recrystd. from MeOH to give 53.5 g. 3-benzyloxy-1-bromobenzene, m. 5963°. BuMgCl, made from 18.5 g. BuCl, 4.8 g. Mg, and 100 ml. tetrahydrofuran, was added dropwise over 1.5 hrs. to 150 ml. tetrahydrofuran which had been saturated 1 hr. with C2H2. During the addition and 15 min. thereafter the addition Of C2H2 was continued, 23.6 g. ethyl 3-oxo-1-pyrrolidinecarboxylate in 50 ml. tetrahydrofuran added over 30 min., the mixture stirred at room temperature 20 min., stirred on a steam bath 30 min., 50 ml. saturated NH4Cl added, the organic layer separated from the viscous mass, the viscous mass extracted with Et2O, and the combined exts. and tetrahydrofuran solution fractionated in vacuo to give 13.7 g. ethyl 3-ethynyl-3-hydroxy-1pyrrolidinecarboxylate. Prepared similarly was: ethyl 3-hydroxy-2-methyl- 3-(2-propynyl)-1-pyrrolidinecarboxylate. Ethyl 3-hydroxy-3-phenyl-1-pyrrolidinecarboxylate (6 g.) in 100 ml. EtOH was hydrogenated in presence of 2 g. 5% Rh-alumina at 3.5 kg./sq. cm. pressure and room temperature to give ethyl 3-cyclohexyl-3-hydroxy-1-pyrrolidinecarboxylate.
IT 94311-45-2P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2,4-diphenyl-, ethyl ester 94384-09-5P, 1-Pyrrolidinecarboxylic acid, 2-(p-chlorophenyl)-4-hydroxy-4-phenyl-, ethyl ester 94384-10-8P, 1-Pyrrolidinecarboxylic acid, 4-(p-chlorophenyl)-4-hydroxy-2-phenyl-, ethyl ester 94577-37-4P, 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-(p-methoxyphenyl)-4-phenyl-, ethyl ester
RL: PREP (Preparation)
(preparation of)
RN 94311-45-2 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2,4-diphenyl-, ethyl ester (7CI) (CA INDEX NAME)

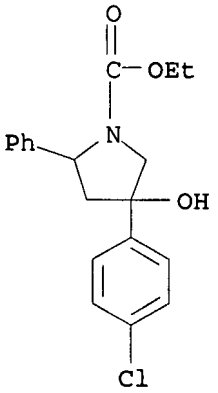


RN 94384-09-5 CAPLUS

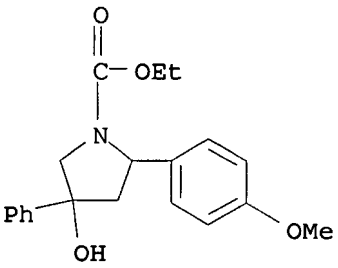
CN 1-Pyrrolidinecarboxylic acid, 2-(p-chlorophenyl)-4-hydroxy-4-phenyl-, ethyl ester (7CI) (CA INDEX NAME)



RN 94384-10-8 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-(p-chlorophenyl)-4-hydroxy-2-phenyl-, ethyl ester (7CI) (CA INDEX NAME)



RN 94577-37-4 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-hydroxy-2-(p-methoxyphenyl)-4-phenyl-, ethyl ester (7CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	222.75	481.92

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-32.76	-32.76

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:09:34 ON 02 MAY 2007